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EPIDEMIC POLIOMYELITIS*

HARRY M. WEAVER†

NEW YORK CITY

ALTHOUGH human poliomyelitis was first described in 1789,[1] anthropologic studies indicate that this disease has afflicted mankind since antiquity.[2] In endemic form, it has been reported from most parts of the world, but in a number of different geographic areas there has been a transition from an endemic disease to one of epidemic character. This transition occurred first in Scandinavia in the 1870's, in Europe in the 1880's, in the northern United States and Australia in the 1890's, in New Zealand in the 1920's, in the southern United States in the 1930's, in the large metropolitan areas of Japan (Osaka and Kobe) in 1938 and 1940, in Mexico and in the British Isles in 1946 and 1947[3] and in a large metropolitan area of India (Bombay) in 1949.

Epidemic poliomyelitis is usually a summer disease, and winter epidemics are relatively rare. On the other hand, poliomyelitis as a sporadic disease occurs throughout all months of the year, and winter epidemics were reported from Malta[4] in 1943 and from Iceland[3] in 1945-46 and again in 1946-47. An especially severe epidemic of poliomyelitis occurred among the Eskimos of Chesterfield Inlet[5] in northern Canada during the winter of 1948-49; its severity may be judged from the fact that there were 57 paralyzed patients and 14 deaths in a total population of 275 persons.

There has been an appreciable increase in the number of cases of poliomyelitis reported from the United States during the past several years. The average number of cases reported per year for the period 1935-39 was 6784. The average for the period 1940-44 was 10,885, and the average for the five-year period 1945-49 was 24,067.

The increased incidence of the disease has been associated with a gradual shift upward in the age group most commonly afflicted. At the turn of the century more than 50 per cent of patients in the cases reported were under two years of age. In the United States at present, from 70 to 80 per cent of the cases occur in persons over the age of five years, and as many as 25 per cent in persons over the age of fourteen. It seems likely that some of this change is due to a shift in the age composition of the population, but the importance of this factor cannot be determined exactly until the 1950 census records become available.

It is suggested that part of the increase in poliomyelitis during recent years may be the result of better recognition of the disease in its nonparalytic form and inclusion, under the term "poliomyelitis," of what must be a large number of cases of "Coxsackie" disease.

Although the viral etiology of poliomyelitis was demonstrated forty-two years ago, adequate funds to support an intensive research effort against the disease did not become available until 1938. This paper presents a brief survey of what this effort has already accomplished and what likely possibilities for control remain to be explored.

In 1938 a chain of events to explain the cause, effects and transmission of poliomyelitis was already established. This chain had four links, the first being that *the disease is caused by a virus*, the second that *the virus, after invading the central-nervous-system, damages or destroys nerve cells*, the third that *the paretic and crippling aftereffects are due to damage to nerve cells rather than to any direct effect of the virus on muscles, bones or joints* and the last that *the disease is transmitted from person to person.*

If this chain of events explains the more important aspects of poliomyelitis, one should be able to control the disease by breaking this chain at any one of several points. From the theoretical point of view this could be achieved by the discovery of some means to eliminate the virus in nature; the finding of some way of preventing contact between man and virus; the development of measures to enable man to resist the nerve-cell-damaging action of the virus with which he comes in contact; the discovery of some agent or treatment that will prevent destruction of nerve cells already damaged as the result of viral invasion of the brain and spinal cord; and provision of better methods of nonspecific treatment to enable the patient with

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†Director of research, National Foundation for Infantile Paralysis, Incorporated.

poliomyelitis to compensate better for loss of function due to destruction of neuromuscular units and the subsequent compensatory changes in muscles, bones and joints.

Progress in Therapy

Approximately 80 per cent of persons in this country have become infected with one or more of the viruses of poliomyelitis by the time they have reached fifteen years of age. In other countries, particularly those with lower standards of living, the percentage of persons infected may be appreciably higher, and the peak rate of infection is usually reached at a much younger age.[6] It has also been shown that of those infected with the virus, recognizable poliomyelitis develops in only a small percentage, and of even this small group, only about half become paralyzed.

Therapy, in the strict sense of the word, concerns treatment after the patient has become infected with the disease-producing agent, as contrasted with prophylaxis, which is descriptive of treatment administered prior to the time of infection. Because there is more interest in preventing paralytic poliomyelitis than in preventing an infection with the virus, it is suggested that the term "therapy" be limited to treatment administered to the patient after onset of the signs and symptoms of the clinical disease rather than after infection with the virus, which in most cases is "silent" and of no deleterious consequence. Therapy in poliomyelitis, according to the definition of the term just suggested, has three objectives: to save lives, to prevent or arrest the progression of paralysis and to minimize crippling.

Nonspecific Therapy

It is now clear that with modern methods of treatment approximately 50 per cent of all patients with the diagnosis of poliomyelitis recover fully and with no apparent aftereffects. Approximately 30 per cent, although afflicted with some residual paralysis, are capable of leading thoroughly useful lives. Approximately 12 per cent suffer extensive paralysis and crippling, and approximately 8 per cent die. These percentages vary slightly from year to year and from place to place.

It seems, from the evidence available, that a patient with poliomyelitis today runs less risk of dying or becoming severely crippled than the patient of former years. However, these results may be more apparent than real. It is not actually known to what extent the results of modern treatment are influenced by the nonspecific effects of better medical and nursing care, or by the more specific effects of moist heat and physical therapy. Furthermore, one cannot see how much modern treatment of poliomyelitis is made to appear more effective than it really is because of inclusion in today's figures of an unknown number of cases of "Coxsackie" disease and a greater number than formerly of patients with nonparalytic cases of poliomyelitis, all or most of whom would have recovered fully without any treatment other than good nursing care.

Although no treatment for poliomyelitis is worthy of the designation "specific," at least five different phases of treatment seem to exert some favorable influence on the end result of the pathologic process:

Bed rest during the pre-paralytic stages of the disease, as contrasted with carrying on normal and particularly strenuous activities, seems to be of some benefit in reducing the amount of paralysis.

After an infection with the virus, nonspecific stresses and strains, such as tonsillectomy, pregnancy, exhaustion and chilling — and perhaps even such minor stresses as trauma and the effects of parenteral inoculations of medicinal and biologic materials — are capable of influencing adversely a person's capacity to resist the more serious forms of the clinical disease. For example, it has been reported that when the virus is present in the community, the risk of poliomyelitis in recognizable form is eight times greater in the pregnant woman than in the nonpregnant woman of the same age group. Under similar circumstances, the risk of recognizable poliomyelitis has been reported to be approximately three times greater in persons whose tonsils and adenoids have been removed within thirty days of onset of the disease, and the risk of the bulbar form of the disease is eleven times greater than normal.[7]

It is known that death in poliomyelitis can and does result from destruction of large numbers of nerve cells in areas of the brain that control such vital functions as respiration. There are, however, many patients who suffer only reversible damage to such cells, and if life can be sustained by artificial means, these cells tend to recover and reassume their functions within a few days or weeks. The availability of better mechanical devices for treating such patients and the more general and intelligent application of improved methods of treatment[8-13] have undoubtedly been responsible for the saving of some lives that formerly would have been lost.

It is also known that fewer persons today than formerly suffer extensive misshapenings of their bodies as a consequence of poliomyelitis. It seems proper to credit this very real advance to improvements in orthopedic surgery, and to the prevention of contractures as the result of more intelligent use of physical therapy.

Everyone is aware of the possibilities, as yet largely untapped, of mental and physical rehabilitation.

It is, I believe, clear that therapy of the kind just discussed is nonspecific, not sufficiently effective to be considered as more than a temporary expedient for the control of poliomyelitis and tremendously expensive to apply.

Inasmuch as there appears to be a distinct limitation, short of satisfaction, to what can be accomplished by nonspecific therapy, attention should be given to what might be accomplished by more specific therapy.

Specific Therapy

Formerly, it was widely believed that a nerve cell was doomed to destruction once it had been invaded by the virus of poliomyelitis. Today, it is known that this is not true. There is evidence that many cells are invaded and even damaged by the virus and yet recover completely without any treatment whatever.[14] Even as late in the process as the first appearance of muscle weakness, many nerve cells, though both already invaded and damaged by the virus, have not yet been destroyed. If an agent can be found that can inactivate the virus within the cell, or can alter the metabolism of the cell so as to arrest further replication of the virus, it is reasonable to hope that paralysis and death as a consequence of poliomyelitis can be greatly decreased. From a practical point of view this should be the prime objective because it permits taking advantage of the immune response that normally follows an infection with the virus and limits the number of persons requiring prolonged treatment.

I am not aware of any chemical or biologic agent that has yet been shown to be capable of achieving this end. There is, however, evidence that neither vaccination nor serotherapy can be of any real benefit if administered after nerve cells have been invaded by the virus.

Progress and Possibilities in Prophylaxis

It has been learned that an infection with the virus of poliomyelitis is an experience common to the vast majority of persons of all races and countries. This is attested to not only by the frequency of isolations of the virus from the excreta of the alimentary canals of human beings but also by the almost universal presence of specific poliomyelitis antibodies in the bloods of adults, and by the age distribution of these antibodies in the bloods of younger groups. There is good reason to believe that the presence of these antibodies constitutes evidence of past infection with the virus. The human infant at birth possesses the same amount of antibody as its mother. These passively acquired antibodies diminish rapidly and disappear within six months to two years if the infant is not exposed to the virus during this period.[15] If, on the other hand, an infection does take place early, the probable result is the production of more antibody without recognizable disease.

It is very likely that the amount of paralytic poliomyelitis reported from a given country is generally in inverse ratio to the percentage of persons with antibodies in their blood, and more especially to the distribution of antibodies in the younger age groups. This suggests, when considered with the further fact that such antibodies are capable of specifically inactivating the virus, that the presence of antibody denotes some measure of immunity to the paralytic disease. It is not yet known whether the immunity conferred by an inapparent infection is absolute or relative, permanent or temporary.

From present knowledge of this subject, it is reasonable to infer that so long as the virus exists, the most effective protection against paralytic poliomyelitis is to be born of a poliomyelitis-resistant mother, and to be exposed to the virus frequently from early infancy through maturity.

It is quite possible that under primitive living conditions, nearly everyone is so protected.[16] In this country, on the other hand, only about 80 per cent of young adults, and presumably pregnant women as well, possesses poliomyelitis antibodies in the blood. Furthermore, not all women possess antibodies to each of the different immunogenic types of the virus capable of inducing the human disease of which there are at least three.[17, 18] Therefore, it is probable that a considerable number of human beings are born without passive protection against the various viruses of poliomyelitis. Moreover, there is some evidence that many people in this country do not become infected with the virus frequently from infancy through adulthood.[15] In view of these findings, it is suggested that the high incidence of paralytic poliomyelitis in this country is probably due to rarity of contacts with the virus and the consequent development of a susceptible state.

A great deal of effort has been devoted to the search for nonhuman hosts or vectors of the virus. All this has yielded negative results except for the demonstration that the virus may sometimes be found in or on flies.[19] It seems, however, that flies play at most only an accessory role in the transmission of the epidemic disease. The negative studies on animals and insects other than flies were concomitant with others showing that the human alimentary tract and excreta serve as an abundant and apparently inexhaustible reservoir of the virus.[20]

Indirect evidence that person-to-person transmission of the virus somehow occurs in the ordinary contacts of daily life[21] continues to accumulate. The exact mechanism of transmission is not clear, but it is obvious that the virus is transmitted easily and rapidly by close personal association of the kind that occurs within households. The virus

of poliomyelitis can be recovered from the alimentary tracts of most members of the household on the very first day that muscle weakness due to poliomyelitis can be detected in any one member of the family unit.[22, 23] This means either that all members of the household are infected simultaneously through some common source or that person-to-person transmission of the virus is very rapid under conditions of close personal association of the kind that occurs within households.

In former years frequent infections with the virus were more or less assured possibly by poor sanitation and large family units,[24] but to gain the blessings of freedom from epidemics and relatively little paralytic poliomyelitis in prior years, plagues of other diseases and lower standards of living had to be accepted. Therefore, to prevent paralytic poliomyelitis today one should try to achieve the result accomplished by nature in the past, possibly through poor sanitation and large families, without paying the penalties of lower standards of living and plagues of other diseases.

From the theoretical point of view this ideal could be accomplished in one of two ways: by preventing infection with the virus or by preventing the paralytic consequences of an infection, while in no way interfering with the transmission of the virus from person to person.

If, by some means as yet unconceived, the virus could be forever and completely eliminated from the world, that would be the ideal solution to human poliomyelitis. If, however, medical science succeeded only in decreasing the number or frequency of infections, as it has probably done already with improved sanitation and smaller families, that would tend to increase rather than to decrease the incidence of paralytic poliomyelitis. It seems, in view of the intimacy of the relation between virus and human beings throughout the world, that it is both wishful and dangerous to think of eradicating paralytic poliomyelitis by eliminating the virus or by preventing contacts between the virus and human beings.

Possibilities of Preventing Paralysis as a Consequence of an Infection with the Virus

Inasmuch as an infection with the virus of poliomyelitis may, under proper circumstances, bestow a measure of resistance to the paralytic disease, there is considerable support for the concept that an infection with the virus is a blessing to be sought after rather than a danger to be shunned. From the theoretical point of view, vaccination, seroprophylaxis and chemoprophylaxis could be effective in preventing the paralytic consequences of an infection with the virus in animal experiments and in man.

Vaccination

It has already been demonstrated experimentally that the usual paralytic consequences of a viral infection of the nervous tissue of monkeys and rodents may be prevented by vaccination with either an inactive or an active virus vaccine.[25] The question today is, "Is it possible to prepare a vaccine against the human disease, and will this vaccine provide a practical means of control?"

In certain diseases — for example, smallpox — an active virus closely related to a virus causing severe human disease has been found that produces only a very mild and transient illness when injected into the human being but protects against a subsequent attack of the more destructive and lethal virus. The question of an active virus vaccine in poliomyelitis is only now receiving serious consideration.

To prepare an effective vaccine with inactive virus one must change active virus to the inactive state, so that it does not have the power to damage nerve cells but does retain its capacity to incite the production of protective antibodies.

Although the paralytic consequences of an infection can be prevented in the animal with an inactive virus vaccine, it must be remembered that protection can be achieved only by the administration of relatively huge quantities of the inactivated virus. It must also be recognized that such vaccines are type specific and that protection against the human disease could be achieved only if the vaccine were to contain all the different immunogenic types of the virus capable of inducing human disease.

One must, of course, bear in mind the possibility of nerve damage as a result of multiple injections of vaccine containing nerve tissue. Perhaps a better source of virus for a vaccine, free of nerve tissue, might be developed as a consequence of a relatively recent discovery that virus can be propagated on non-nervous tissue.[26, 27] This is still only a possibility, since to date relatively small quantities of virus have been produced by this method.

The duration of immunity that might follow administration of a poliomyelitis vaccine is not known. There is, however, suggestive evidence from other diseases that duration of immunity is much longer when induced with an active virus vaccine than with an inactivated preparation, and that a given level of immunity can be achieved with less expenditure of virus when an active virus vaccine is employed.

Practically no work has been done to determine the most effective time and route of vaccination. If it is true that one can best achieve resistance to the paralytic disease by being born of a mother possessing antibodies against the virus, and by subsequently coming into contact with the virus at frequent intervals from early infancy through adult-

hood, vaccination should be most successful if carried out during early infancy; or, if postponed until later life, it might be combined with immune serum or human gamma globulin.

Thus, although it is true that the paralytic consequences of an experimental infection with the virus of poliomyelitis can be prevented by vaccination, a considerable number of hurdles must be overcome before a practical vaccine against the human disease can be achieved. Investigators are, however, closely approaching the time when continued work in the field of vaccination must be almost entirely dependent upon human trials. In the not too distant future the experimental models with which they have been working in the past will have been exhausted.

Seroprophylaxis

Prevention of the paralytic consequences of an infection with the virus of poliomyelitis has also been achieved experimentally by passive immunization with poliomyelitis antiserums administered prior to the time of invasion of nerve cells.[28] Perhaps I should repeat that there is no convincing evidence that any poliomyelitis antiserums, however effective, would have an appreciable beneficial effect after infection of nerve cells has taken place.[29] Antibodies ordinarily do not enter cells, and it is probably in the cell that the virus multiplies.[30]

If it is true that most people have escaped the paralytic consequences of poliomyelitis by being born of mothers possessed of antibodies, and by subsequently coming into contact with the virus frequently from early infancy through adulthood, a similar condition could be brought about artificially by administration of gamma globulin during the times when poliomyelitis is usually prevalent. However, the institution of this procedure at present is not advisable because it is not known if a given antibody level might prevent an infection with the virus. Indiscriminate administration of gamma globulin to large masses of the population might result in prevention of infection and transient immunity only for a very few weeks after administration of the serum. This, of course, would lead to a population devoid of active immunity, which results from infections with the virus.

Studies are now under way to determine the answer to the following questions: What is the rate of elimination of poliomyelitis antibodies administered to human beings in the form of human gamma globulin or hyperimmune animal serums? Is it possible to prevent an alimentary-tract infection with the virus by passive immunization with gamma globulin? What level of antibody is required to prevent paralysis but allow infection with the virus?

Until these studies have been completed, it would seem to be unwise to carry out large-scale human experimentation with parenteral injections of human gamma globulin in the hope of preventing paralytic poliomyelitis. It is, however, believed that the principle on which such experiments is based is worthy of further investigation.

Chemoprophylaxis

From a theoretical point of view, prevention of the paralytic consequences of an infection with the virus of poliomyelitis might also be achieved by chemoprophylaxis. This might reasonably be expected to work in one of two ways: by inactivating the virus wherever it might be in the body, or by changing the metabolism of the nerve cell to such an extent as to provide an unsuitable site for virus propagation.

To date, the hope for a practical chemoprophylactic agent against human poliomyelitis is based mainly on success with certain rickettsial and viral infections other than poliomyelitis, and to a certain extent on the effectiveness of some agents against the poliomyelitis virus itself. The amount of the effect against the virus of poliomyelitis and the toxicity of the drugs that are of value is such, however, that use of these agents in human poliomyelitis is not justified. It is believed, however, that there is more than adequate evidence to justify more intensive research in the field of chemoprophylaxis than has heretofore been supported.

Summary

Although the program of research against poliomyelitis has not as yet provided a practical means of control for the human malady, it has produced a vast store of knowledge about the human and experimental forms of the disease. This research has cleared up much of the confusion that existed twelve years ago, and has produced sufficient knowledge to permit definition of the lines of attack that might reasonably be expected to provide a means of control for the human disease.

It appears to be consistent with present knowledge to say that there is little reason to hope that the virus can be eliminated from the environment or that human exposure to it can be effectively prevented. It is equally doubtful that much can be accomplished through serotherapy. It has been learned that complete recovery from poliomyelitis can be ensured only if destruction of nerve tissue by the virus can be prevented.

Although it is true that present methods of nonspecific therapy have saved lives and reduced the amount of crippling, there is no prospect that such treatment, however much it is improved, can prevent destruction of nerve tissue. There is, however, much support for the statement that control of human poliomyelitis is attainable through chemotherapy, chemoprophylaxis and seroprophylaxis and vaccination. Some of these have already been proved to be effective against the experimental form of the disease. The major problem today is to

determine which, if any, of these might provide a practical means of control for the human disease.

References

1. Underwood, M. *A Treatise on the Diseases of Children.* Second edition. 2 vol. Vol. 2. *Debility of the Lower Extremities.* 339 pp. London: J. Mathews, 1789. Pp. 53-57.
2. International Committee for the Study of Infantile Paralysis. *Poliomyelitis.* 562 pp. Baltimore: Williams & Wilkins Co., 1932.
3. Stowman, K. Incoming tide of poliomyelitis. *Epidemiol. & Vital Statistics Rep.* **1**:6, 1947.
4. Seddon, H. J., Agius, T., Bernstein, H. G. G., and Tunbridge, R. E. Poliomyelitis epidemic in Malta, 1942-3. *Quart. J. Med.* **14**:1-26, 1945.
5. Peart, A. F. W., et al. Outbreak of poliomyelitis in Canadian Eskimos in wintertime. *Canad. J. Pub. Health* **40**:405-419, 1949.
6. Sabin, A. B. Epidemiology of poliomyelitis: problems at home and among armed forces abroad. *J. A. M. A.* **134**:749-756, 1947.
7. Anderson, G. W., Anderson, G., Skaar, A. E., and Sandler, F. Risk of poliomyelitis after tonsillectomy. *Ann. Otol., Rhin. & Otolaryn.* **59**:602-613, 1950.
8. Wright, J. Respir-aid rocking bed in poliomyelitis. *Am. J. Nursing* **47**:454, 1947.
9. Sarnoff, S. J., Whittenberger, J. L., and Hardenbergh, E. Electrophrenic respiration. *Am. J. Physiol.* **155**:1-9 and 203-207, 1948.
10. Bower, A. G. Concept of poliomyelitis based on observations and treatment of 6000 cases in four-year period. *Northwest. Med.* **49**: 103-107, 187-190 and 261-266, 1950.
11. Brown, J. B., Baker, A. B., and McQuarrie, I. Bulbar form of poliomyelitis. II. Therapeutic measures based on pathologic and physiologic findings. *J. A. M. A.* **135**:425-428, 1947.
12. Galloway, T. C., and Seifert, M. H. Bulbar poliomyelitis: favorable results in its treatment as problem in respiratory obstruction. *J. A. M. A.* **141**:1-8, 1949.
13. Stimson, P. M. Treatment of acute poliomyelitis together with some suggestions on diagnosis. *J. Pediat.* **31**:82-92, 1947.
14. Bodian, D. Virus, nerve cells, and paralysis: study of experimental poliomyelitis in spinal cord. *Bull. Johns Hopkins Hosp.* **83**:1-106, 1948.
15. Aycock, W. L., and Kramer, S. D. Immunity to poliomyelitis in mothers and newborn as shown by neutralization test. *J. Exper. Med.* **52**:457-464, 1930.
16. Aycock, W. L., and Meadors, G. F. Principles of variolation as exemplified by subclinical immunization in poliomyelitis in cooler and warmer climates. *Am. J. M. Sc.* **215**:296-310, 1948.
17. Bodian, D., Morgan, I. M., and Howe, H. A. Differentiation of types of poliomyelitis viruses. III. Grouping of fourteen strains into three basic immunological types. *Am. J. Hyg.* **49**:234-245, 1949.
18. Kessel, J. F., and Pait, C. F. Differentiation of three groups of poliomyelitis virus. *Proc. Soc. Exper. Biol. & Med.* **70**:315, 1949.
19. Paul, J. R., Trask, J. D., Bishop, M. B., Melnick, J. L., and Casey, A. E. Detection of poliomyelitis virus in flies. *Science* **94**:395, 1941.
20. Francis, T., Jr., Brown, G. C., and Penner, L. B. Search for extrahuman sources of poliomyelitis virus. *J. A. M. A.* **136**:1038-1093, 1948.
21. Gordon, F. B., Schabel, F. M., Jr., Casey, A. E., and Fishbein, W. I. Laboratory study of epidemiology of poliomyelitis. *J. Infect. Dis.* **82**:294-301, 1948.
22. Wenner, H. A., and Tanner, W. A. Widespread distribution of poliomyelitis in households attacked by disease. *Proc. Soc. Exper. Biol. & Med.* **66**:92-94, 1947.
23. Brown, G. C., Francis, T., Jr., and Ainslie, J. D. Studies of distribution of poliomyelitis virus. V. Virus in familial associates of cases. *J. Exper. Med.* **87**:21-27, 1948.
24. Hammon, W. Immunity in poliomyelitis. *Bact. Rev.* **13**:135-159, 1949.
25. Morgan, I. M. Immunization of monkeys with formalin-inactivated poliomyelitis viruses. *Am. J. Hyg.* **48**:394-406, 1948.
26. Enders, J. F., Weller, T. H., and Robbins, F. C Cultivation of Lansing strain of poliomyelitis virus in cultures of various human embryonic tissues. *Science* **109**:85-87, 1949.
27. Evans, C. A., and Green, R. G. Extraneural growth of poliomyelitis virus: its significance relative to possible methods of prevention. *J. A. M. A.* **134**:1154, 1947.
28. Kramer, S. D. Protection in white mice with human post-convalescent serum against infection with poliomyelitis virus (Armstrong strain). *J. Immunol.* **47**:67-76, 1943.
29. Bahlke, A. M., and Perkins, J. E. Treatment of preparalytic poliomyelitis with gamma globulin. *J. A. M. A.* **129**:1146-1150, 1945.
30. *Viral and Rickettsial Infections of Man.* Edited by T. M. Rivers. 587 pp. Philadelphia: J. B. Lippincott Co., 1948. P. 10.

ABSCESS FORMATION IN MYOCARDIAL INFARCTION*

C. G. Tedeschi, M.D.,† Thomas D. Stevenson, Jr., M.D.,‡ and Herbert M. Levenson, M.D.§

BOSTON AND FRAMINGHAM, MASSACHUSETTS

In 1933, Cossio and Berconsky[1] reported a case of coronary occlusion with myocardial infarction in which an abscess was found in the infarcted area at post-mortem examination. As far as we could ascertain, this is the only report in the medical literature of this unusual complication of myocardial infarction.

The patient of Cossio and Berconsky was a sixty-four-year-old man who complained of the symptoms considered characteristic of myocardial infarction: severe precordial pain, weakness and a sense of impending death. The patient was hospitalized on the fourth day of illness and treated symptomatically. The signs of a bronchopneumonic process developed and he died on the fourteenth hospital day. Post-mortem examination revealed a bronchopneumonia due to a pneumococcus, and the same type of organism was identified in a myocardial abscess localized within the area of the myocardial infarct.

*From the Department of Pathology, Boston University School of Medicine, and the Division of Laboratories, Framingham Union Hospital.

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†Instructor in pathology, Boston University School of Medicine; director of laboratories, Framingham Union Hospital.

‡Assistant surgeon (R), United States Public Health Service.

§Assistant in medicine, Boston University School of Medicine; visiting physician, Framingham Union Hospital.

A pulmonary infection is a frequent complication in elderly cardiac patients who are confined to bed as in the case mentioned above. A bacteremia is prone to develop under these circumstances, but its signs are often obscured by the cardiac and pulmonary symptoms and the clinical course is frequently terminated before the bacteria produce metastatic abscesses.

Though abscess of the myocardium is rare, its occurrence may be expected whenever pyemia is present. Saphir,[2] in an analysis of 240 cases of myocarditis, arrived at the conclusion that myocardial abscess is not too rare in the presence of pyemia and, in itself, is not of great significance but indicates the severity of the underlying infection. Weiss and Wilkins[3] found 31 cases of myocardial abscess in the autopsy records of the Boston City Hospital. In 2 of the 31 cases perforation of the heart had occurred. Thirty-two additional cases among 5626 autopsies (0.56 per cent) at the Michael Reese Hospital were reported by Saphir.[4] Flaxman[5] noted 29 cases of myocardial abscess in 14,160 autopsies performed at the Cook County Hospital from 1929 to 1942 (0.2 per cent). According to Gladden[6] 10 cases of myocardial abscess followed

by rupture of the heart had been reported up to 1943. In the series of Weiss and Wilkins[3] and Flaxman[5] the staphylococcus was the commonest pathogenic organism found in the abscess.

Although it seems that the necrotic tissue of a myocardial infarct might predispose to the invasion of the area by pathogenic organisms with subsequent abscess formation, the report of Cossio and Berconsky[1] remains as an isolated observation of this unique complication of myocardial infarction. Since data on the actual frequency of this condition and the details of its pathogenesis are not available, a careful study of all infarcts observed post mortem has been undertaken. The 2 cases reported below are the first that have come to our attention showing abscess formation and pathogenic organisms at the site of a myocardial infarct. Rupture of the heart with hemopericardium occurred in 1.

Case Report

Case 1. J. W., a 69-year-old woman, was admitted to the hospital in coma. Four days prior to entry she had experienced a severe pain in the region of the shoulder blades that radiated to both arms. A physician advised complete bed rest, but this advice was not heeded and shortly before admission the patient suddenly lapsed into coma.

The family history was noncontributory.

The past history was significant in that a portion of the right colon had been resected 2 years prior to the present illness because of a diverticulitis. The postoperative course had been complicated by a thrombophlebitis and a pulmonary embolism. Medical consultation had revealed cardiac enlargement, hypertension and an abnormal electrocardiogram consistent with coronary-artery disease.

Physical examination disclosed a comatose, elderly, obese woman with rapid and shallow respirations. The skin was pale, cold and moist and mottled areas of cyanosis were present. The cervical veins were dilated. The heart was enlarged to percussion, and on auscultation the heart sounds were distant but no murmurs were heard. The remainder of the physical examination, including neurologic examination, was negative.

The temperature was 101.8°F., the pulse unobtainable, and the respirations 30. The blood pressure was also unobtainable.

Examination of the blood showed a red-cell count of 4,180,000, with a hemoglobin of 14.3 gm., and a white-cell count of 16,900, with 81 per cent neutrophils. The hematocrit was 42 per cent. Urinalysis demonstrated a specific gravity of 1.018, with a negative test for sugar and an albumin of 100 mg. per 100 cc. On microscopical examination the sediment was loaded with white cells, but no casts or red cells were seen. The nonprotein nitrogen was 69 mg., and the blood sugar 207 mg. per 100 cc. The blood Hinton reaction was negative.

An electrocardiogram showed a Q_3T_3 pattern consistent with an acute posterior myocardial infarct.

With supportive therapy and parenteral administration of fluid the patient regained consciousness, and the state of peripheral circulatory collapse concomitantly improved. The radial pulse and blood pressure became obtainable (the blood pressure was 180/80), and it was noted that the pulse was paradoxical in character. The temperature remained elevated, and the signs of a bronchopneumonic process appeared at the left base on the 2nd hospital day. Peripheral circulatory collapse reappeared, and the patient died on the 3rd hospital day.

Post-mortem examination, performed 5 hours after death, led to the following pathological diagnoses: occlusion of the main-stem right coronary artery; myocardial infarction, abscess formation and rupture of the posterior wall of the left ventricle; hemopericardium; generalized arteriosclerosis; pulmonary edema, bilateral, diffuse; bronchopneumonia, disseminated, left lung; passive congestion of the liver and spleen; fibrous adhesive peritonitis, diffuse; arteriosclerotic kidney, bilateral; healed end-to-end ileotransverse anastomosis of the colon; and laparotomy scar, healed. Only the cardiac lesion is reported in detail.

The cardiac area was greatly enlarged, and when the pericardial sac was opened, it was found to contain 600 cc. of partially clotted blood.

The parietal pericardium was blood tinged but smooth and glistening throughout. The epicardium was normal in appearance over the anterior aspect of the heart but glassy and coated with a thin layer of fibrinous exudate in the posterior aspect, where an irregularly shaped tear, 1.8 cm.

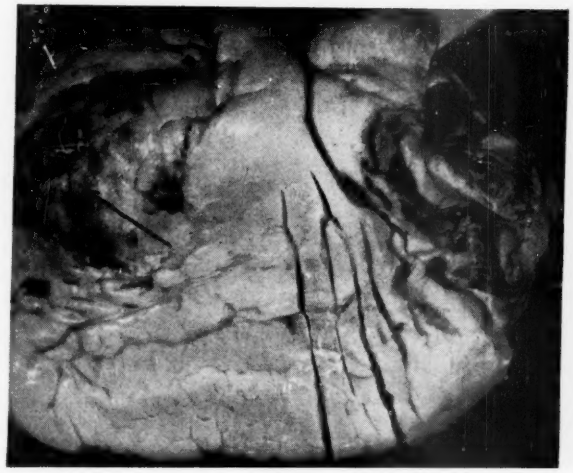

Figure 1. *Photograph of the Specimen, Showing the Tear in the Middle Third of the Left Ventricle.*

in the largest dimension, was noticeable at the middle third of the left ventricle (Fig. 1). The tear involved the entire thickness of the myocardium so that a probe could be passed through it into the left ventricular cavity without resistance. The surrounding myocardium was infiltrated by blood and flabby in consistence in an area about 6 cm. in diameter. Externally and on cut section this area displayed a variegated tinge from reddish brown to yellowish gray. Clusters of honey-combed pockets, each pin head in size or larger, were scattered throughout this area. Grossly, these pockets were suggestive of small abscesses and contained a thick, golden-yellow material.

The coronary arteries were diffusely narrowed, with atheroma formation and calcification. The right coronary artery was occluded a short distance below its main stem by a firmly adherent, friable, yellowish-brown thrombotic mass. Examination of the cardiac chambers revealed a laminated thrombus on the posterior aspect of the left ventricle.

At the site of the myocardial infarct the microscopical sections showed an almost complete obliteration of the normal architecture. The muscle fibers displayed loss of striations and of nuclear patterns and seemed fused together into an amorphous mass of eosinophilic material. The capillaries in the area were congested, and extravasated red cells were present throughout. There was a concomitant marked infiltration of polymorphonuclear leukocytes either scattered or in clusters, and this extended into the epicardium. The leukocytes were not well preserved; the majority were fused together or showed karyorrhexis and karyolysis resulting in a scattering of cellular débris (Fig. 2). The endocardial mural thrombus consisted of amorphous eosinophilic material and was interspersed with white cells and cellular débris. The mural thrombus merged indistinctly into the adjacent necrotic myocardium. The thrombotic mass in the lumen

of the right coronary artery showed incipient organization with intimal histiocytic and fibroblastic proliferation and atheromatous changes.

Cultures from the left ventricular cavity and the left ventricular wall at the site of infarction yielded a pure culture of coagulase-positive, hemolytic *Staphylococcus aureus*; the same organism, *Neisseria catarrhalis* and a nonhemolytic streptococcus were obtained in cultures from the bronchopneumonic foci in the left lung. Sections from the myocardial infarct stained by the Gram-Weigert method showed clusters of gram-positive cocci (Fig. 3).

CASE 2. E. W., a 75-year-old man with schizophrenia of the paranoid type, had been an inmate of a mental institution for 40 years. Four years prior to the final illness he was found to have a systolic hypertension (blood pressure of

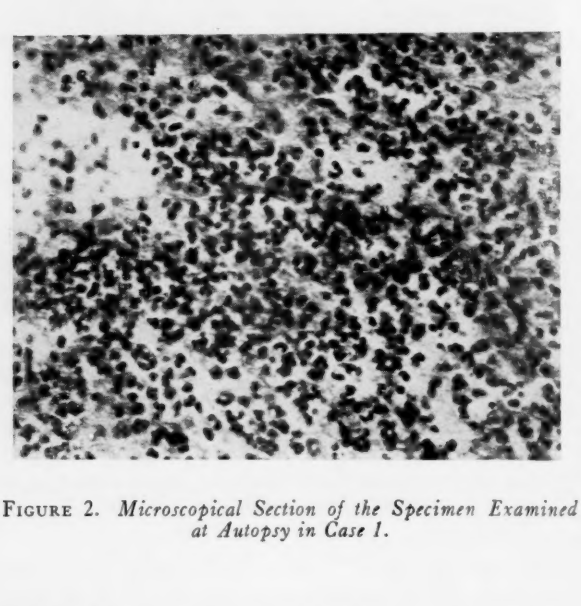

FIGURE 2. *Microscopical Section of the Specimen Examined at Autopsy in Case 1.*

200/80). The final illness was initiated by the complaint of severe chest pain, but the patient's mental status and deafness made the evaluation of the symptoms difficult. He was confined to bed because of the persistence of the chest pain, and although he was apprehensive he did not appear to be in any acute distress. A productive cough and fever (temperature of 103.8°F.) appeared, and terminally peripheral circulatory collapse was present. He died suddenly on the 4th day after the onset of the chest pain.

At post-mortem examination, performed 6 hours after death, the pathological diagnoses were as follows: myocardial infarction; thrombosis of the anterior descending branch of the left coronary artery; generalized arteriosclerosis; pulmonary congestion, diffuse, with bilateral basilar bronchopneumonia; fibrous adhesive pleurisy; passive congestion of the liver and spleen; cholelithiasis; arteriosclerotic kidney, bilateral; cerebral arteriosclerosis, with fibrous thickening of the pial meninges; focal softening in the right cerebellar hemisphere and in the right temporal lobe; and mild internal hydrocephalus. The description of the heart only is reported in detail.

The heart was enlarged, weighing 420 gm., but was not unusual in shape. The coronary arteries were tortuous, and diffuse atheromatous plaques with calcification narrowed the vessel lumens. Serial sections through the coronary tree revealed a 0.5-cm. area of the left anterior descending branch to be occluded by an adherent grayish thrombus.

The apical region of the myocardium was mottled in appearance. Over the apex the epicardium had a glassy appearance and was coated with a thin layer of fibrinous exudate. When the cardiac chambers were opened, the apical area of the heart was thin, flabby in consistence and hemorrhagic. In the same area a number of small cavities were seen either scattered or in clusters and ranging in size from 0.1 to 0.3 mm. in diameter, and were filled with greenish-yellow material. These abscess-like areas involved the entire myocardium, but the endocardium and the epicardium were spared. Laminated thrombi were present over the mural endocardium. There were recent thrombotic vegetations on the mitral leaflets, which also showed marginal thickening and fibrosis.

In the microscopical sections from the infarct the myocardium had a glassy appearance and stained brick red (hematoxylin and eosin stain). Nuclei and striations were absent in this area. Red-cell extravasations were present in places, and many polymorphonuclear leukocytes were interspersed between the necrotic muscle fibers. The leukocytes were packed together in places, and their outlines were indistinct. A scattering of cellular débris was also present in the same area.

Cultures from the infarcted area yielded a nonhemolytic streptococcus and a coagulase-positive hemolytic *Staph. aureus*. A staphylococcus with the same characteristics was present in the cultures from the bronchopneumonic foci in the lungs.

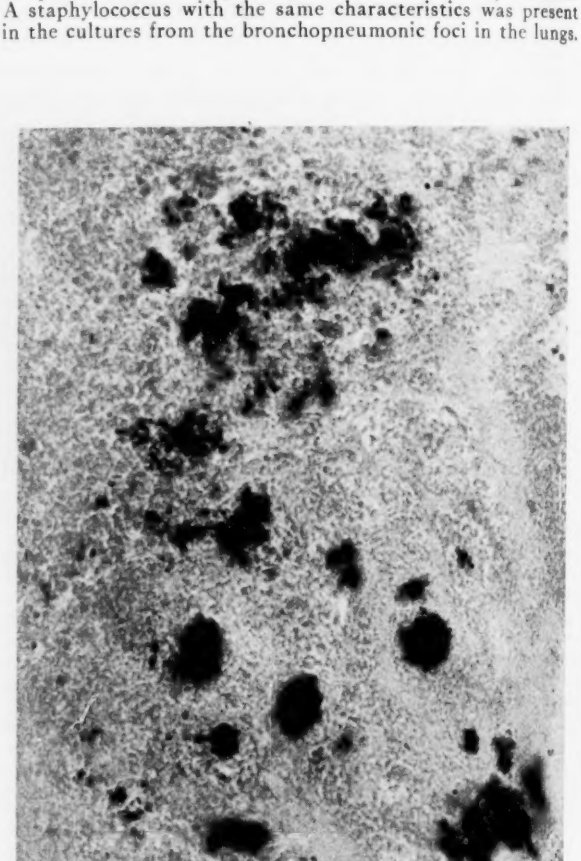

FIGURE 3. *Clusters of Gram-Positive Cocci in the Necrotic Myocardium in Case 1 (Gram-Weigert Stain x930).*

Clusters of gram-positive cocci were identified in the microscopical sections from the infarct stained by the Gram-Weigert technic.

DISCUSSION

The cases reported above had a number of features in common. The patients were elderly persons with severe generalized arteriosclerosis, and both had suffered a coronary occlusion with myocardial infarction in which an abscess was found post mortem; bronchopneumonia was an additional complicating factor. Seven days ensued between the onset

of symptoms and death in the first case, and four days in the second. Case 1 was further complicated by rupture of the heart at the site of infarct and abscess formation with a resulting cardiac tamponade.

The common point of interest was the presence of an abscess at the site of the myocardial infarct in both cases, similar to the case reported by Cossio and Berconsky.[1] In both cases a virulent staphylococcus was present in the abscess, and organisms with similar characteristics were found in the bronchopneumonic foci in the lungs. The common identity of the organisms found in the areas of suppuration in the heart and in the lungs makes one inclined to suspect a connection between the processes in these organs. The nature of the organisms and their cultural and pathogenic characteristics preclude the possibility of contamination of the medium or post-mortem bacterial invasion.

It is well known that the vessels adjacent to any acute local infection are affected by the inflammatory process. As the vessel wall becomes involved, intimal damage is followed by platelet adherence with subsequent thrombus formation. This process contributes to the extension of the infection and tissue necrosis. That this mechanism is inadequate to explain the pathology of these 2 cases is demonstrated by the striking absence of inflammatory reaction in the wall of the vessels at the site of occlusion that is invariably found when a vessel is involved by a septic process. In addition the septic process was limited to the area of infarction. Another possibility is that the occlusion of the vessel was the result of a septic embolus, with subsequent infarction and abscess formation. This seems quite remote since the occlusive mass in the coronary artery was a typical thrombus and no sources of emboli were found except for the mural thrombi in the ventricular walls, which are rarely the source of emboli involving the coronary arteries. Finally, no abscesses could be demonstrated in the other organs as generally occur when septic emboli are present in the blood stream. A theory that seems more consistent with the pathology observed is that the abscess was the result of the invasion of a primarily bland myocardial infarct by circulating micro-organisms. The absence of any other source of infection and the similarity of the organisms obtained from the myocardial abscess and the bronchopneumonic foci point to the pneumonic process as the likely source of the terminal bacteremia. A pathogenesis and a resulting pathology similar to that conceived for these secondarily infected infarcts has been presented elsewhere by one of us[7] in an attempt to interpret wedge-shaped foci of septic necrosis in the lungs, grossly resembling ischemic infarcts, which could also be traced to the bacterial invasion of primarily bland pulmonary infarcts.

Since the results of systematic investigation are not available it is not possible to predict the frequency of this complication of myocardial infarction. The presence of an infectious process in some part of the body and a subsequent bacteremia are prerequisites to its development.

The paucity of reports of this condition in the literature indicates that the invasion of a myocardial infarct by pathogenic bacteria followed by abscess formation is an extremely rare event. The practical implications of this complication — that is, the interference with healing of the infarct and the enhanced danger of rupture of the myocardium — warrant a thorough investigation of the problem. It is being investigated in our own material and it is one of the purposes of this report to stimulate similar investigation by those who have access to larger material.

Summary

Two cases in which abscess formation and the presence of pathogenic organisms at the site of a myocardial infarct were demonstrated at autopsy are reported. Rupture of the heart and hemopericardium occurred in 1 case. In both, a coagulase-positive hemolytic *Staphylococcus aureus* was the organism isolated from the abscess. A concomitant bronchopneumonia was present in both cases, and an organism similar to that present in the abscess was isolated from the lung. It is suggested that the septic foci in the myocardium resulted from the invasion of a primarily bland infarct by circulating micro-organisms. The necrotic tissue and circulatory stasis of the infarcted area provided suitable conditions for the lodgment and growth of the bacteria. The absence of any other source of infection and the similarity of the organisms isolated from the heart and lungs point to the bronchopneumonia as the source of the terminal bacteremia.

References

1. Cossio, P., and Berconsky, I. Absceso parietal del corazón e infarto del miocardio. *Semana med.* **2**:1691-1698, 1933.
2. Saphir, O. Myocarditis: general review, with analysis of 240 cases. *Arch. Path.* **32**:1000-1051, 1941.
3. Weiss, S., and Wilkins, R. W. Myocardial abscess with perforation of heart. *Am. J. M. Sc.* **194**:199-205, 1937.
4. Saphir, O. Myocarditis: general review, with analysis of 240 cases. *Arch. Path.* **33**:88-137, 1942.
5. Flaxman, N. Myocardial abscess. *J. A. M. A.* **122**:804-806, 1943.
6. Gladden, J. R. Myocardial abscess with perforation of heart following staphylococcal pyemia. *Am. J. Surg.* **60**:277-285, 1943.
7. Tedeschi, C. G. Focolai cuneiformi di bronchopolmonite. *Boll. d. Soc. med.-chir. di Modena* **34**:31-67, 1934.

THE EFFECTS OF CORTISONE ON THE COURSE OF ACUTE GLOMERULONEPHRITIS*

Report of a Case

CHARLES H. BURNETT, M.D.,† MONTE A. GREER, M.D.,‡ BELTON A. BURROWS, M.D.,§ JOHN H. SISSON, M.D.,¶ ARNOLD S. RELMAN, M.D.,|| LOUIS A. WEINSTEIN, M.D.,† AND CHARLES G. COLBURN, M.D.**

BOSTON

THE report of the beneficial influence of Cortisone on the course of acute rheumatic fever[1] prompted the trial of this hormone in the treatment of acute glomerulonephritis. This paper describes complete clinical and laboratory findings in a patient with acute glomerulonephritis who received 200 mg. of Cortisone daily for twelve days. Although renal function transiently improved, a definitely beneficial effect on the course of the disease was not demonstrated.

METHODS

Most of the procedures are described in another report.[2, 3] Additional methods included quantitative estimation of formed elements and of protein in the urine[4]; and serum and urine complement (alexin).[5] During the forty-three-day period that the patient was studied, he was on the metabolism service of the Evans Memorial and received a constant diet of the estimated composition given below. The electrolyte intake varied appreciably only on the three days on which renal clearance was measured when, incident to Tm_{PAH} (tubular secretion of para-aminohippurate) determinations, sodium intake was augmented as much as 188 milliequiv. per day.

TABLE 1. *Intake and Output, Blood and Urine Data.*

DATE	CORTISONE	FLUID INTAKE	BODY WEIGHT	HEMOGLOBIN	WHITE-CELL COUNT	EOSINOPHILS	COMPLEMENT* 50 PER CENT	NONPROTEIN NITROGEN	CARBON DIOXIDE
	mg./24 hr.	*cc./24 hr.*	*lb.*	*gm./100 cc.*	*x10³*	*per cu. mm.*	*units/cc.*	*mg./100 cc.*	*milliequiv./liter*
12/28/49...	—	4190	116	13.0	10,000	—	—	—	—
12/29	—	3970	115	—	—	—	27	—	—
12/30/49† .	—	4553	117	—	—	—	—	—	—
12/31	—	4920	116	—	—	—	25	—	—
1/1/50 ...	—	3520	117	—	—	—	—	—	—
1/2/50 ...	—	3465	117	—	—	—	25	—	—
1/3	—	3240	117	11.7	4,700	—	—	36	—
1/4	200	3785	116	11.0	6,125	127	25	—	27
1/5	200	3490	117	11.8	15,000	—	27	34	27
1/6	200	3400	117	11.5	13,850	35	25	—	—
1/7	200	3500	117	—	—	—	35	40	30
1/8	200	3640	118	—	—	—	36	—	—
1/9	200	3500	118	—	—	26	35	33	30
1/10	200	3500	118	—	—	—	31	—	—
1/11	200	3560	118	—	—	43	35	34	30
1/12	200	3540	118	—	—	—	18	—	—
1/13	200	3440	118	11.1	16,400	69	26	38	—
1/14	200	3390	118	—	—	—	36	—	—
1/15	200	3260	118	—	—	—	18	—	—
1/16‡	100	4171	117	8.9	18,950	13	18	32	30
1/17	—	3440	117	—	—	—	16	—	—
1/18	—	3465	118	—	—	70	22	39	26
1/19	—	3500	118	10.3	7,700	—	19	—	—
1/20	—	3405	116	—	—	447	23	36	30
1/21	—	3460	115	—	—	332	18	—	—
1/22	—	3760	113	—	—	—	25	—	—
1/23	—	3500	113	—	—	—	25	36	30
1/24	—	3865	112	—	—	—	27	—	—
1/25	—	3590	113	—	—	211	—	34	30
1/26	—	3500	116	—	—	—	—	—	—
1/27§	—	4335	—	—	—	202	26	37	27

*Urine was examined on numerous occasions for complement, but it was never present.

†Renal clearance on this day; 188 milliequiv. of sodium given in infusion, in addition to diet.

‡Renal clearance on this day; 149 milliequiv. of sodium given in infusion, in addition to diet.

§Renal clearance on this day; 164 milliequiv. of sodium given in infusion, in addition to diet.

CASE REPORT

A. C. (E.M.H. 341191), a 15-year-old boy of Italian descent, was transferred from another hospital on December 21, 1949. The onset of the illness 4 weeks previously had

*From the Evans Memorial and the Haynes Memorial, Massachusetts Memorial Hospitals, and the Department of Medicine, Boston University School of Medicine.

This work was done under contract with the Army Medical Research and Development Board, and during the tenures of a Life Insurance Medical Research Fellowship, a Postdoctorate Fellowship, National Heart Institute, and a Research Fellowship in the Medical Sciences, National Research Council.

†Associate professor of medicine, Boston University School of Medicine.

‡Assistant resident in medicine, Evans Memorial, Massachusetts Memorial Hospitals.

§Life Insurance Medical Research Fellow.

¶Postdoctorate research fellow, United States Public Health Service.

||Fellow in medical sciences, National Research Council.

**Research fellow, Haynes Memorial, Massachusetts Memorial Hospitals.

been characterized by a shaking chill, fever and coryza. These symptoms subsided in 5 days, and he returned to school. From the 10th to the 12th day after the initial illness, he had a steady, sharp, nonradiating pain in the right costovertebral angle. During the next week the urine became "rusty" colored; definite facial and periorbital edema and questionable ankle edema appeared. Nine days prior to admission a diagnosis of acute nephritis was made, and the patient was admitted to another hospital on the following day. On a low-protein, salt-free regimen, a profuse diuresis ensued, with gradual subsidence of edema and a weight loss of 16 pounds in 8 days. The blood pressure was 160/110 on admission, fell in four days to 130/80, and remained at approximately that level thereafter. A palpable spleen and generalized lymph-node enlargement were noted. The urine gave a + to ++ test for albumin, and the sediment contained varying numbers of red and white cells. The maximum urinary specific gravity was 1.025. The blood urea nitrogen on admission was 13 mg. per 100 cc.

The patient was transferred to the Evans Memorial for study on December 21. The family history was noncontributory. The past history was irrelevant; there had been no sore throat within the past year, and no history of scarlet fever, tonsillitis, rheumatic fever, chorea or urinary complaints was elicited.

Physical examination was entirely negative except for many shotty anterior and posterior cervical lymph nodes, a firm, nontender spleen, which descended 1 or 2 cm. below the right costal margin on inspiration, and a 5-mm., raised ulcerated lesion on the hard palate, just to the right of the midline. The ocular fundi were normal; and there was no peripheral edema.

The pulse was 92, the temperature 98.2°, and the respirations 12; the blood pressure was 110/61.

Urinalysis showed a pH of 5.0, a specific gravity of 1.019, and a ++++ test for albumin, and the sediment contained 10 leukocytes and 75 to 100 erythrocytes per high-power field and an occasional granular and red-cell cast. The blood hemoglobin was 14.0 gm. per 100 cc., the hematocrit 44 per cent, and the erythrocyte sedimentation rate 40 mm. in 1 hour (Wintrobe method). The white-cell count was 9600, with 63 per cent neutrophils and no abnormal lymphocytes on smear. The blood nonprotein nitrogen was 67 mg., and the total protein 8.4 gm. per 100 cc., with an albumin of 4.5 gm. and a globulin of 3.9 gm. per 100 cc. Beta-hemolytic streptococci grew from three nose and throat cultures. X-ray films of the abdomen and chest were within normal limits, as were two electrocardiograms taken during the first 2 weeks. Phenolsulfonphthalein excretory capacity on December 23 was 20 per cent in 15 minutes, 31 per cent in 30 minutes, 49 per cent in 1 hour and 61 per cent in 2 hours.

The patient was kept at rest in bed and was given a constant daily diet estimated to contain 3132 calories, 355 gm. of carbohydrate, 148 gm. of fat, 95 gm. of protein, 50 milliequiv. of sodium and 125 milliequiv. of potassium. From January 4, 1950, until discharge, 1.8 gm. of ferrous gluconate was administered daily. The entire hospital course was asymptomatic; the lymphadenopathy and palatal lesion gradually disappeared although the spleen remained palpable until discharge.

One hundred milligrams of Cortisone was given intramuscularly every 12 hours for a 12-day period from January 4 to 16. The salient features of the patient's course are presented in Table 1 and Figure 1. Renal clearances were measured 5 days before initiation of, on the last day of and 11 days after the end of Cortisone therapy (Tables 2 and 3).

Daily Addis counts and urinary protein determinations prior to Cortisone administration demonstrated a slight, though somewhat variable tendency for the formed elements and protein of the urine to diminish. After the renal clearance on December 30, there was a moderate increase in red-cell and protein excretion although the number of urinary leukocytes continued to decrease and remained quite low during the remainder of the hospital stay. On the day after institution of Cortisone therapy, an exacerbation occurred. The temperature, previously normal, rose to 101°F. during the first 24 hours on the drug, but the febrile reaction subsided in 3 days. The proteinuria increased significantly during the 3rd to 5th days of treatment and returned to the pre-

TABLE 1 (*Concluded*).

DATE	SERUM SODIUM	SERUM POTASSIUM	URINARY VOLUME	URINARY PROTEIN	WHITE CELLS IN SEDIMENT	RED CELLS IN SEDIMENT	URINARY SODIUM	URINARY POTASSIUM
	milliequiv./liter	*milliequiv./liter*	*cc./24 hr.*	*gm./24 hr.*	*million/24 hr.*	*million/24 hr.*	*milliequiv./24 hr.*	*milliequiv./24 hr.*
12/28/49 ..	—	—	3170	—	—	—	29	106
12/29	—	—	2550	<0.5	48	118	14	124
12/30†	138	4.3	4277	0.5	18	46	94	124
12/31	—	—	3750	0.5	18	240	21	78
1/1/50 ...	—	—	2500	—	—	—	30	101
1/2/50 ...	—	—	2600	0.8	9	561	12	87
1/3	—	—	2220	0.8	14	220	11	123
1/4	138	4.7	2570	0.5	10	956	13	116
1/5	137	4.5	2360	0.5	6	446	14	100
1/6	—	—	2070	1.9	16	1642	5	75
1/7	138	4.8	2800	1.2	12	2046	6	87
1/8	—	—	2680	1.5	20	1960	5	111
1/9	142	5.0	2410	0.9	26	2446	4	117
1/10	140	5.1	2070	0.5	14	1488	5	90
1/11	142	4.8	2750	0.5	9	783	9	135
1/12	144	4.6	2455	0.5	7	667	9	120
1/13	143	4.7	2190	0.4	4	484	9	124
1/14	—	—	2440	0.9	3	486	16	128
1/15	—	—	2270	0.4	5	511	12	125
1/16‡	143	4.0	2714	0.8	8	392	61	145
1/17	—	—	2370	0.4	8	274	51	97
1/18	141	4.2	3230	0.5	0	22	96	103
1/19	140	4.3	4030	0.4	10	394	158	108
1/20	144	4.8	2340	0.4	0	304	139	70
1/21	147	5.1	3950	0.4	2	364	204	154
1/22	—	—	2970	—	—	—	61	107
1/23	142	4.7	2960	<0.1	0	205	18	137
1/24	143	4.8	3150	0.3	4	692	8	140
1/25	141	4.5	1751	0.3	2	332	7	89
1/26	142	4.5	3125	0.3	1	179	9	166
1/27§	143	4.2	2719	0.3	0	610	88	126

vious level in six days. The hematuria progressively increased, a peak of 2,500,000,000 red cells per 24 hours being reached on the 5th day of Cortisone, and gradually fell to the previous level by the 9th day. No cause for this exacerbation other than the Cortisone administration could be found. The possibility that the renal-clearance test was responsible was considered, but since 5 days had elapsed between the day of test and the appearance of increased proteinuria, this explanation seemed unlikely. When Cortisone was stopped the proteinuria and hematuria continued to diminish, but were still present at the time of discharge.

The only other significant clinical effect of Cortisone was the development of swelling and redness of the face during the last few days of therapy. Blood chemical measurements were normal before Cortisone was started and were unchanged thereafter. Urinary potassium excretion was essentially unaffected, but significant retention of sodium and a 2-lb. weight gain developed during Cortisone administration. A marked increase in excretion of water and sodium and a concomitant weight loss occurred during the 5 days after treatment was stopped. Leukocytosis and eosinopenia were demonstrable during therapy, disappearing after it was stopped.

The serum complement (alexin) levels were low prior to the institution of Cortisone therapy. Three days after the beginning of treatment, there was a rise in the serum content of alexin that was maintained for about 5 days although at no time did the concentration reach a normal level. This alexin increase was roughly correlated with the increase in the number of erthryocytes and the quantity of protein excreted in the urine. During the latter part of Cortisone administration and after this agent was stopped, the alexin content returned, with occasional exceptions, to levels observed before the hormone was started. No complement was detected in the urine at any time.

Daily determinations of the serum level of antistreptolysin varied between 833 and 2000 units, indicating a recent infection with the beta-hemolytic streptococcus, and there were no significant alterations in titer associated with Cortisone therapy. Frequent examination of the urine revealed no antistreptolysin.

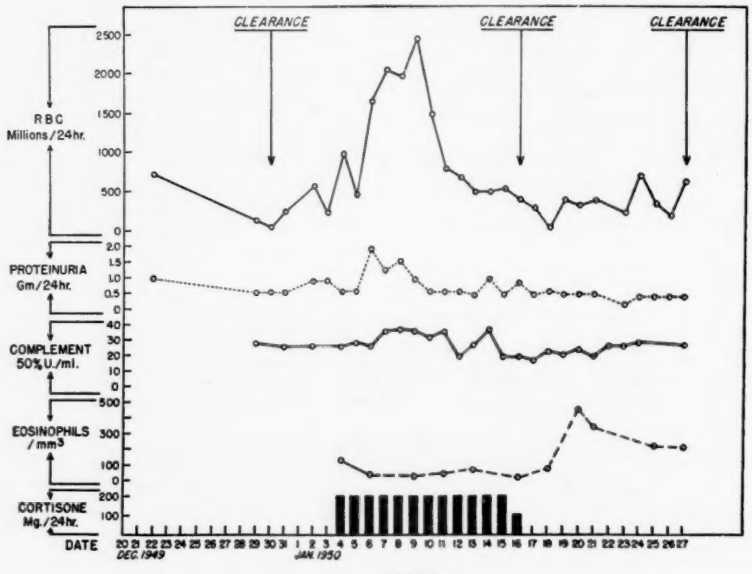

FIGURE 1. *Diagram, Showing the Salient Features of the Patient's Course in the Hospital.*

During control renal-clearance measurements, the clearances of inulin and sodium para-aminohippurate were significantly depressed, and Tm_{PAH} was slightly lower than normal. On Cortisone there were significant increases in all three of these functions. Eleven days after withdrawal of the drug inulin clearance and Tm_{PAH} returned to control values; the clearance of para-aminohippurate and renal blood flow showed continued improvement. Hence the filtration fraction was normal during control periods and on Cortisone, and fell to a subnormal level after the hormone was stopped. The ratio of inulin clearance to Tm_{PAH}, on the other hand, was low initially, rose on Cortisone and returned almost to control levels on the final test (Table 2).

Clearance of sodium and the ratio of sodium to inulin clearance increased slightly during Cortisone therapy and

TABLE 2. *Average Renal Clearances (Not Corrected for Surface Area*).*

DATE	TREATMENT	INULIN CLEARANCE	PAH CLEARANCE	FILTRATION FRACTION	RENAL BLOOD FLOW	Tm_{PAH}	RATIO OF INULIN CLEARANCE TO Tm_{PAH}	HEMATOCRIT
		cc./min.	*cc./min.*	%	*cc./min.*	*mg./min.*		%
12/30/49	Control	73	380	19.2	620	66	1.10	38.7
1/16/50	Cortisone therapy for 12 days	105	477	22.0	716	83	1.27	33.4
1/27/50	11 days after Cortisone withdrawal	81	604	13.4	958	69	1.17	36.9

*Surface area, 1.57 square meters.

returned to control levels on the third test (Table 3). These increases were noted despite the fact that day-to-day sodium excretions had demonstrated sodium retention (Table 1). There were also significant increases in clearances of phosphate and uric acid, and the same effects on clearance of potassium. Clearances of creatinine rose progressively throughout the period of observation. However, the ratio of creatinine to inulin clearance fell from 136 per cent during control observations to 101 per cent on Cortisone, and rose again to 135 per cent after the drug was stopped.

After discharge, the patient was seen at monthly intervals in the outpatient department. By March 2 the proteinuria had disappeared; by May 24 the urine was entirely free of abnormal elements, including red blood cells. When he was last seen on May 25 there was no evidence of residual renal damage.

TABLE 3. *Relations of Plasma Concentrations, Clearances and Ratio of Inulin Clearances to Clearance of Sodium, Potassium, Phosphate, Creatinine and Uric Acid.*

DATE	TREATMENT	CONSTITUENT	PLASMA CONCENTRATION	CLEARANCE	RATIO OF ELECTROLYTE CLEARANCE TO INULIN CLEARANCE
				cc./min.	%
12/30/49	Control	Sodium	136.0 milliequiv. per liter	0.2	0.3
		Potassium	4.2 milliequiv. per liter	24.0	33.0
		Phosphate	[illegible] mg. per 100 cc.	17.0	23.0
		Creatinine	1.4 mg. per 100 cc.	99.0	136.0
		Uric acid	5.2 mg. per 100 cc.	11.0	15.0
1/16/50	Cortisone therapy for 12 days	Sodium	142.0 milliequiv. per liter	0.5	0.5
		Potassium	4.0 milliequiv. per liter	40.0	38.0
		Phosphate	6.5 mg. per 100 cc.	23.0	22.0
		Creatinine	0.9 mg. per 100 cc.	106.0	101.0
		Uric acid	3.4 mg. per 100 cc.	17.0	16.0
1/27/50	11 days after Cortisone withdrawal	Sodium	142.0 milliequiv. per liter	0.1	0.1
		Potassium	4.1 milliequiv. per liter	32.0	40.0
		Phosphate	5.1 mg. per 100 cc.	13.0	16.0
		Creatinine	0.8 mg. per 100 cc.	109.0	135.0
		Uric acid	5.1 mg. per 100 cc.	9.0	11.0

DISCUSSION

It is very questionable whether Cortisone exerted any beneficial effects on this patient with acute glomerulonephritis. Thorn et al.[6] recently reported similar results, and Farnsworth, using ACTH, believed that 2 patients in the acute phase of the disease were benefited.[7] It should be noted that both these observers considered the nephrotic syndrome to be sometimes favorably influenced by ACTH of Cortisone.[6, 8] The data on the patient reported above suggest that Cortisone produced a transient exacerbation — as evidenced by fever, increased hematuria and proteinuria, and a rise in serum complement. Since a coincidental reactivation cannot be excluded, it is also possible that the entire course was consistent with that seen in many cases of acute glomerulonephritis.

The levels of and the changes in serum complement observed in this patient resemble those noted in a number of patients in the acute phase of glomerulonephritis.[9-11] It is difficult to state whether the rise following administration of Cortisone was significant. A low concentration of complement may be the result of failure in production, increased rate of destruction or fixation by combinations of homologous antigen and antibody. The low level prior to treatment and the rise following the administration of Cortisone may have been due to an effect on any one of these three mechanisms for control of alexin level. Since glomerulonephritis is thought to be caused by some antigen-antibody combination, as yet unknown, one can speculate that Cortisone may have released this combination in part and thus allowed some of the fixed complement to become free.

Studies of antistreptolysin titers in the serum revealed only that the patient had had recent infection with the beta-hemolytic streptococcus. Cortisone had no effect on the serum levels of this antibody.

The changes in renal clearances indicate a definite improvement of kidney function during Cortisone administration. It is entirely possible that the improved filtration rate, the increased filtration fraction and the increased ratio of inulin clearance to Tm_{PAH} reflect a beneficial effect on the inflammatory lesion of glomerulonephritis, and that inulin clearance and Tm_{PAH} fell after Cortisone was withdrawn because the favorable influence of the hormone was no longer operating. The continued improvement in para-aminohippurate clearance and renal blood flow after the hormone was stopped could then be interpreted as being part of the natural course of the disease. The pattern of a low inulin clearance and filtration fraction on the last test after Cortisone had been omitted has previously been observed in acute glomerulonephritis.[12] On the other hand, the changes in renal function that occurred in this patient during Cortisone administration have also been observed in normal persons receiving both ACTH and Cortisone, and in patients with Addison's disease and hypertension and vascular disease to whom Cortisone was given.[2] The authors suggested that these changes in renal hemodynamics were either direct effects of the hormones on renal function or decreases in hematocrit that regularly occurred in their patients. Since similar hematocrit changes occurred in this patient, the possibility must be entertained

that these alternative explanations for changes in renal function were also operative here. There is therefore the distinct possibility that the changes in renal function were nonspecific and unrelated to any beneficial effect of Cortisone on the disease. The fact that hematuria and proteinuria actually increased during administration of the hormone could support the latter interpretation. The changes in clearances of sodium, potassium, phosphate, creatinine and uric acid, and in clearance ratios of these substances to inulin clearance are similar to those observed in normal persons.[13]

Summary

A case of acute glomerulonephritis in which 200 mg. of Cortisone was given daily for twelve days is described.

Proteinuria and the number of formed elements in the urine did not decrease with Cortisone; indeed a transitory increase in these elements suggested that the hormone had a deleterious effect.

Serum complement levels tended to be lower prior to Cortisone, and rose in association with the increase in hematuria and proteinuria.

Inulin clearance was low, and Tm_{PAH} (tubular secretion of para-animohippurate) was normal or slightly low during initial studies; both rose on Cortisone and returned to control levels after the hormone had been withdrawn. Para-aminohippurate clearance and renal blood flow, low initially, showed progressive improvement throughout the course. These changes were possibly due to a favorable influence of this hormone on the pathologic process. It seems more probable that they reflected the effects of Cortisone on renal function per se, rather than on the inflammatory lesion, and changes consistent with the natural course of the disease.

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References

1. Hench, P. S., et al. Effects of adrenal cortical hormone 17-hydroxy-11-dehydrocorticosterone (compound E) on acute phase of rheumatic fever: preliminary report. *Proc. Staff Meet., Mayo Clin.* **24**: 277-297, 1949.
2. Relman, A. S., et al. Unpublished data.
3. Burnett, C. H., Relman, A. S., Burrows, B. A., Ingbar, S. H., and Sisson, J. H. Unpublished data.
4. Addis, T. *Glomerular Nephritis: Diagnosis and treatment.* 338 pp. New York: Macmillan Co., 1948.
5. Fischel, E. E., Pauli, R. H., and Lesh, J. Serological studies in rheumatic fever. II. Serum complement in rheumatic state. *J. Clin. Investigation* **28**:1172-1181, 1949.
6. Thorn, G. W., Merrill, J. P., Smith, S., Roche, M., and Frawley, T. Clinical studies with ACTH and cortisone in renal disease. *Arch. Int. Med.* **86**:319-354, 1950.
7. Farnsworth, E. B. Acute and subacute glomerulonephritis modified by adrenocorticotropin. *Proc. Soc. Exper. Biol. & Med.* **74**:57-59, 1950.
8. *Idem.* Metabolic changes associated with administration of adrenocorticotropin in nephrotic syndrome. *Proc. Soc. Exper. Biol & Med.* **74**:60-62, 1950.
9. Longcope, W. T. Study of bacteriolytic serum complements in disease: contribution to our knowledge of terminal and other infections. *J. Hyg.* **3**:28-51, 1903.
10. Kellett, C. E. Complement titre in acute nephritis: with special reference to causation by reversed anaphylaxis. *Lancet* **2**:1262-1265, 1936.
11. Kellett, C. E., and Thomson, J. G. Complementary activity of blood serum in nephritis. *J. Path. & Bact.* **48**:519-531, 1939.
12. Earle, D. P., Jr., Taggart, J. V., and Shannon, J. A. Glomerulonephritis: survey of functional organization of kidney in various stages of diffuse glomerulonephritis. *J. Clin. Investigation* **23**:119-137, 1944.
13. Ingbar, S. H., et al. Unpublished data.

CLINICAL NOTE

MECKEL'S DIVERTICULUM AS AN ABDOMINAL EMERGENCY

BYRON V. WHITNEY, M.D.*

BANGOR, MAINE

SINCE the description of Meckel's diverticulum by Johann Frederic Meckel in 1809, much has been written about this entity. It is therefore unnecessary to discuss all the pathologic conditions that may be caused by the persistence of the proximal or intestinal end of the vitelline duct, which connects the yolk sac with the midgut. The purpose of this paper is to present a case in which a gangrenous Meckel diverticulum produced partial obstruction of the small intestine. The point to be stressed is the difficulty that arises in correct diagnosis.

CASE REPORT

A 22-year-old man complained of pain in the upper portion of the abdomen, accompanied by nausea and vomiting for 2 days. He indicated the epigastrium as being the area of most severe pain but said that the abdomen was sore all over. The bowel movements had been normal up until the present illness. He had had no bowel movement since the onset of this illness. There had been no hematemesis, melena or history of stomach trouble. No urinary symptoms were present. The complaints became more severe up until the time of admission.

Two weeks previously, while attending college, he had had a similar illness. He was admitted to the hospital with a diagnosis of questionable appendicitis. Further study ruled out this diagnosis. He remained at the hospital for 24 hours, during which he received fluids intravenously and morphine. After this period of treatment he was apparently well, and was discharged from the hospital.

The past history and history of the systems were irrelevant.

The positive findings on physical examination were confined to the abdomen and the oral cavity. The mucous membranes of the mouth were very dry. The abdomen was not distended, but was somewhat full. Tenderness was present throughout but was more prominent in the epigastrium. There was referred pain from the lower abdomen to the supraumbilical area. Muscular spasm, which was observed throughout the abdomen, was especially prominent in the epigastrium. Peristalsis was diminished, but not absent.

Examination of the blood disclosed a red-cell count of 5,640,000, with a hemoglobin of 108 per cent, and a white-cell count of 20,350, with 80 per cent neutrophils, 40 per cent band forms and 16 per cent lymphocytes. The blood amylase was 88 units per 100 cc. The urine was normal except for 0.01 per cent albumin and a + test for acetone.

Wangensteen drainage was started with a Levine tube, and fluids were given intravenously to combat the dehydration. In view of the physical findings, it was decided that an acute condition of the abdomen was present and that operative intervention was necessary. The preoperative diagnosis was a ruptured viscus, probably acute appendicitis with rupture.

At operation serosanguineous fluid was found in the peritoneal cavity. Another interesting finding was several coils of small intestine contained within the circle of a Meckel diverticulum, which was coiled upon itself and bound to another portion of the small intestine. The diverticulum was 7 cm. in length and 2.2 cm. in diameter. It was dark red, swollen and soft in consistence. The coils of the intestine that were involved in the obstruction were edematous and dark red, but when the obstruction was relieved they returned to a pink color in a very short while. The diverticulum was excised, and the opening in the ileum closed by means of a purse-string suture of No. 000 plain catgut, a continuous running suture of No. 000 plain catgut and an interrupted layer of No. 0000 cotton sutures. The suturing was done along the longitudinal surface of the ileum, thus leaving ample intestinal lumen below the line of the suture. The appendix was found to be 8.5 cm. in length and 0.6 cm. in diameter, and was located in a retrocecal position. It was not pathologic and was removed in routine fashion.

Postoperatively the patient did very well. He was given fluids intravenously, 100,000 units of regular penicillin every 3 hours and streptomycin, 0.5 gm. every 6 hours for 7 days, and kept on Wangensteen suction for 4 days. He was eating well and having normal bowel movements by the 7th day. A gastrointestinal series showed no signs of obstruction or other abnormality. The final diagnosis was inflammation of a Meckel diverticulum, resulting in partial obstruction of the small intestine.

This case was particularly interesting for two reasons: the presence of epigastric pain as the outstanding symptom and the history of a similar illness two weeks previously. Gastrointestinal series would not have aided in the diagnosis of this case at the first episode of abdominal pain, since the pathologist reported that the lumen of the Meckel diverticulum was only pin point in size.

*Surgeon, Eastern Maine General Hospital.

156 State Street

Correction. In the Medical Progress report by Dr. Allan M. Butler entitled "Diabetic Coma," which appeared in the October 26 issue of the *Journal*, the word "millimols" in the ninth line of the final paragraph in the first column on page 651 and in the next to last line of the third paragraph of the second column on the same page should be changed to read "milliosmoles." On page 655, in the sixth line of the paragraph numbered "1" under the heading "*Provision of Parenteral Fluid Therapy*," the words "45 milliequiv." should be changed to read "40 milliequiv."

MEDICAL PROGRESS

SEROLOGIC TESTS IN THE DIAGNOSIS OF INFECTIOUS DISEASES (Concluded)

JOHN C. AYRES, M.D., M.P.H.,* AND ROY F. FEEMSTER, M.D., DR.P.H.†

BOSTON

Arthropod-Borne Virus Encephalitides and Lymphocytic Choriomeningitis

A large group of neurotropic virus infections of man, frequently encountered in epidemic form, are grouped as arthropod-borne virus encephalitides, since the viruses have been isolated from mosquitoes, ticks or mites.[62] The following viruses belong to this group: St. Louis, western equine, eastern equine, Venezuelan equine, Japanese B, Russian Far East and louping-ill.

Most of the diseases in this group range in severity from the mildest type of illness, which gives no indication of primary involvement of the central nervous system, through a mild febrile meningitic form with spinal-fluid changes and other clinical manifestations, like those of nonparalytic poliomyelitis, to a severe central nervous disease characterized by stupor, tremors, convulsions, coma and death.[63] The more severe cases are those usually recognized. In some of the infections of man there may be a fleeting viremia, or the virus may be present in the spinal fluid. If the disease is fatal, an opportunity of isolating the virus from the central-nervous-system tissue may be afforded. In many infections, even the pathological lesions are so similar that the etiology cannot be determined by microscopical study alone. However, in most of these infections, serologic methods only are available for laboratory diagnosis.

Two types of tests are available for the diagnosis of this group of diseases: virus neutralization and complement fixation. The former has been the favored test for many years; however, newer knowledge regarding the effect of temperature and of storage on certain antibodies has necessitated re-evaluation of the comparative methods previously considered reliable.[64] The complement-fixation test is relatively new in this field. The antigens used, although vastly improved,[65-67] vary greatly in potency and specificity, and sometimes even become anticomplementary after relatively short periods of storage.[68] A large amount of work has been done with hyperimmune animal serums[69, 70]; however, there has been little study of human patterns of response and only for a few viruses.[68, 71-76] Obviously, the technics of both tests must be improved before there can be complete confidence in their results.

TABLE 2. *Average Human Immunologic Pattern in Certain Virus Infections.**

VIRUS	TYPE OF TEST	WEEKS AFTER ONSET						YEARS AFTER ONSET	
		0–1	1–2	2–3	3–4	7–8	15–16	1	2
Western equine	Neutralization	++	++++	+++++	+++++	+++++	+++++	++	+
	Complement fixation	0	±	+	++	+++	++	±	0
St. Louis	Neutral	0	±	+	++	+++	++++	++	+
	Complement fixation	±	+	+++	++++	++++	++++	+	±
Japanese B	Neutralization	±	±	±	+	++	+++	++	+
	Complement fixation	0	+	+++	++++	+++	+++	+	?
Lymphocytic choriomeningitis	Neutralization	0	0	±	±	+	++	+	+
	Complement fixation	0	+	++	++	++	++	±	0

*Based on data of Hammon.[77]

The times of appearance and wane of neutralizing antibodies are entirely different from those of complement-fixing antibodies[77] (Table 2). These differences, when both tests are performed, can be of great practical value when understood. For instance, since complement-fixing antibodies for western equine virus disappear one or two years after infection, the presence of neutralizing antibodies only may mean a past infection with the virus or an early stage of the infectious process. If, in a St. Louis type of infection, a single serum sample, taken between the twelfth and the twentieth day, contained complement-fixing antibodies without neutralizing antibodies, this would mean an infection with St. Louis virus of recent onset. The eastern equine variety behaves much like the western equine virus.

*Assistant director, Division of Communicable Diseases, Massachusetts Department of Public Health.

†Director, Division of Communicable Diseases, Massachusetts Department of Public Health.

Because of antigenic differences in strains of the same virus, marked differences in the degree of response and time of development of antibodies with different viruses and the lability of antibody under certain storage conditions, it is difficult to set significant lower limits for a positive neutralization test. However, a neutralization index of 1 to 9 is generally regarded as negative, one of 10 to 49 as equivocal, and one of 50 or above as positive.[6]

Two or more serums are essential for a diagnosis by the complement-fixation test. The time and degree of rise should be in approximate accordance with that shown in Table 2. In most serums taken thirty or more days after onset, titers of 1:8 to 1:64 will be obtained; however, the response can be greater or less. Since St. Louis, Japanese B and West Nile viruses are antigenically related, there will be some cross-reaction; however, antibodies for a homologous virus are, as a rule, at a higher level than those for heterologous agents. It is highly advisable that both neutralization and complement-fixation tests be performed on the same serums.

Infectious Mononucleosis

Infectious mononucleosis is one of the "great imitator" diseases, since it can be confused with a variety of conditions, such as diphtheria, typhoid, leukemia, syphilis, serum sickness, measles, erythema nodosum, typhus and brucellosis, as well as other, less important diseases. Although bacterial, protozoal and viral causes have been described, definite proof for any one causative agent is not available. In 1932 Paul and Bunnell[80] demonstrated a consistent and marked increase in sheep-cell agglutinins in the serums of patients with infectious mononucleosis. Previously, similar sheep-cell agglutinins had been described in the serums of normal persons[78] and of those with serum sickness.[79] However, it was subsequently found that sheep-cell agglutinins of infectious mononucleosis could be differentiated easily from those of serum sickness and of normal serum by differential adsorption with guinea-pig kidney and beef red blood cells.[80-82] Sheep-cell agglutinins in normal serum and in serum sickness are adsorbed and removed by guinea-pig kidney, whereas beef red blood cells adsorb the agglutinins from serum in both serum sickness and infectious mononucleosis.

Sheep-cell agglutinins in infectious mononucleosis are present in low titer during the first week of illness, but, by the second and third weeks, the titer is usually quite high, falling off sharply by the fifth week. Agglutinin titers of 1:320 or higher in the absence of serum therapy are indicative of infectious mononucleosis. However, serum from suspicious cases should be examined at an interval of five to seven days to determine rise in titer. Agglutinins may be present in normal serum to a titer of 1:160 and in serum sickness to a titer of 1:20,480. Both these agglutinins may be removed by adsorption with guinea-pig kidney. Failure of guinea-pig kidney to affect sheep-cell agglutinin titer of a patient's serum is indicative of infectious mononucleosis. Final confirmation can be obtained by removal, with beef erythrocytes, of the agglutinins remaining after adsorption with guinea-pig kidney. Should a partial drop in titer occur after adsorption with guinea-pig kidney, both infectious mononucleosis and serum sickness may be present; however, it might be remembered that persistence of sheep-cell agglutinins in the blood has been demonstrated a year or more after treatment with horse serum.[83]

Influenza

The methods used in influenza diagnosis to demonstrate a rise in antibody titer between paired serums are the neutralization tests in mice or chick embryos,[84, 85] the complement-fixation test[86, 87] and the agglutination-inhibition test.[80-90] These procedures give results that correlate well with one another. Since the agglutination-inhibition test is the simplest to perform, it is most commonly used. On the other hand, the neutralization tests are rarely used in routine work, for they require more time and expense and give little information not obtainable by the in vitro tests.

Influenza, as it occurs today, is the result of infection, primarily with either of two antigenically unrelated virus types — namely, A and B. However, each type contains many strains, all of which are antigenically related to a greater or lesser degree, some being quite dissimilar. As a result of this wide spectrum of strain antigenicity, the specificity and sensitivity of serologic tests vary directly with the antigenic relations between the test virus and the infecting virus. However, the PR8 strain of influenza A[91] and the Lee strain of influenza B,[92] when used as test viruses, have been found to give satisfactory results and are therefore most commonly employed. Ideally, a strain from the outbreak of illness in question would be the most sensitive in detecting antibody rises.

Since the antibody titer begins to rise between six and ten days after the onset of an infection, the acute-phase serum should be taken not later than the fifth day. A maximum is reached in two or three weeks, after which the level begins to decline; hence, the convalescent-phase specimen should be taken from the tenth to the fourteenth day after onset. A diagnosis might still be made with second specimens taken after a month or more.

A fourfold increase in antibody titer from an acute-phase to a convalescent-phase serum is considered to be significantly diagnostic of influenza. Almost all persons have circulating antibodies for influenza A and B at the onset of any infection, because of the wide prevalence of the viruses and the use of vaccination. Titers in serums from sup-

posedly normal persons cover a wide range, including very high levels. Hence, significant titer limits cannot be set, nor can a single specimen of high titer be considered significant. A significant rise in titer against one of the virus types is highly diagnostic, for no false-positive results have been reported as yet. Occasionally, small rises are found against the other type of virus,[93] but this may be due to an anamnestic response or a small sprinkling of the other virus in an epidemic predominantly of one type. Confusion may arise also through the use of influenza vaccines, since the antibody response to parenterally injected virus cannot be differentiated from that due to virus infection. Vaccination should be suspected whenever an antibody response occurs to both types of virus.

During epidemic periods, 60 to 80 per cent of cases clinically diagnosed as influenza will show a significant antibody response. Many of the remaining patients who fail to show a significant response may still have influenza, and the lack of response may be from any number of causes. They may be poor reactors, or they may have such high initial antibody levels at the onset that the production of a considerable amount of antibody may be obscured by that already present. There may be a variation in the specificity of response, and a critical rise may be demonstrated when another test strain is used. On the other hand, other agents may be producing a similar illness.

Mumps

Until recently, no specific laboratory methods have been available for the diagnosis of mumps or its complications. Lately, it has become possible to obtain serologic evidence of any type of mumps infection by demonstrating the appearance or increase of mumps antibody by the use of the complement-fixation[94-97] or the hemagglutination-inhibition test.[98] The complement-fixation test is the one most commonly employed.

The complement-fixation test can be used to determine the immunity status of a person against mumps[99] and to establish the diagnosis, especially in meningoencephalitis with absence of salivary-gland involvement.[100] The presence of antibody, even at a very low concentration as indicated by a weak fixation (1+ in 1:2 dilution) is indicative of a previous infection and the existence of immunity. The demonstration of a fourfold increase in antibody concentration during the course of an illness is conclusive evidence of a mumps infection. When the parotid gland is involved, antibody first appears, usually five to seven days after the appearance of glandular swelling and almost always by the end of the second week. The antibody may persist for years in the circulating blood, but in a concentration lower than that reached during convalescence. In cases in which the first specimen has not been obtained sufficiently early to permit the demonstration of a rise in titer, the finding of titers exceeding 1:64 (1:192 final dilution) can be interpreted as suggestive of recent infection, for they rarely occur in the serums of normal persons, except in those infected within the preceding year.

The demonstration of a fourfold increase in the titer of antihemagglutinins during the course of illness may be interpreted as being due to mumps virus[98]; however, the test is not as satisfactory as the complement-fixation test. The antihemagglutinins tend to appear two or three days after the complement-fixing antibodies and persist at a higher titer for a longer time.

The skin test is rarely of diagnostic value, since it becomes positive in most persons several weeks after the onset of mumps. However, it plays an important role in the interpretation of serologic tests, since the inoculation of skin-test antigens can initiate or stimulate the production of complement-fixing antibody in persons not suffering from the disease.[101] Hence, skin testing should not be done for diagnosis, but should be reserved for determining immunity status.

Primary Atypical Pneumonia

To a large extent, the diagnosis of primary atypical pneumonia is one of exclusion. There are no specific laboratory tests available, since the agent has not as yet been isolated and characterized. However, two nonspecific laboratory tests have been found to be useful adjuncts in the differential diagnosis late in the course of illness. They are the tests for cold hemagglutinins and agglutinins for *Streptococcus MG*.

Basis for the cold hemagglutination test is the observation that convalescent-phase serums from many cases of primary atypical pneumonia contain agglutinins for human Group O erythrocytes that are operative at temperatures below 37°C. Cold hemagglutinins begin to appear late in the first week of illness or during the second week, reach a maximum from the middle of the second to the middle of the fourth week and disappear or are present in considerably decreased titer from the fourth to the sixth week.[27] The titer of cold hemagglutinins is generally proportional to the severity of the disease as judged by the symptomatology, extent of pulmonary lesion and height and duration of the fever. However, only 50 per cent of patients on the average develop demonstrable cold hemagglutinins,[102] but the figures have varied widely.

There are several satisfactory methods of demonstrating cold agglutinins,[103-105] and titers of 1:32 or 1:64 are generally considered significantly abnormal. Titers of 1:128 to 1:1024 or more are not often seen except in primary atypical pneumonia or in certain hemolytic anemias. More important than a single serum titer is the demonstration of a fourfold increase in titer during the course of ill-

ness. Cold hemagglutinins are not pathognomonic of primary atypical pneumonia, for they have been described in trypanosomiasis, black-water fever, mumps orchitis, hemolytic anemias, certain liver diseases, peripheral vascular diseases, a variety of the common respiratory diseases and others.[26, 104-108] However, most of these diseases are easy to differentiate, and primary atypical pneumonia is the only respiratory disease yielding high titers.

Streptococcus MG was first isolated from the lungs in a fatal case of primary atypical pneumonia,[109] but it has since been isolated also from the upper respiratory tracts of normal persons and those with nonpneumonic acute respiratory disease.[108, 110] However, the organism has been isolated more frequently in cases of primary atypical pneumonia than in any of the other acute respiratory diseases.[102] The part that *Streptococcus MG* plays in the mechanism of primary atypical pneumonia is unknown,[102, 111] but it has been observed that convalescing patients develop agglutinating antibodies for this organism in their blood and their detection in convalescent-phase serums is of value in the differential diagnosis.[110, 112-116] Antibodies begin to appear by the second or third week after onset and reach a maximum during the fourth and fifth weeks. Antibodies for *Streptococcus MG* can be correlated with the severity of the illness as the cold hemagglutinins can; however, the two types of antibody are not related,[110] and one can be detected without the other's being present. Agglutinin titers for *Streptococcus MG* of 1:20 or more may be found in 50 per cent of the cases on the average. Low titers may be found in normal persons, in various acute respiratory diseases and in certain streptococcal infections. Demonstration of a fourfold or greater increase during the course and convalescence of the disease is most significant.

Psittacosis-Lymphogranuloma-Venereum Group

The psittacosis-lymphogranuloma-venereum group is a term applied to a group of viruses that are similar in morphologic and staining characteristics and share certain antigenic components. Included in this group are the viruses of psittacosis,[117] ornithosis,[118, 119] meningopneumonitis,[120] human pneumonitis (strains S.F.,[121] Louisiana[122] and Illinois[123]), spontaneous mouse pneumonitis,[124-126] feline pneumonitis,[127] lymphogranuloma venereum[128, 129] and, finally, the less definitely related viruses of trachoma and inclusion blenorrhea (inclusion conjunctivitis). The group appears to be intermediate between the viruses and rickettsias; and the family name of *Chlamydozoaceae* in the genus of *Miyagawanella* has been proposed.[130]

There is no simple means for differentiating the infective agents of psittacosis of birds and man, lymphogranuloma venereum of man and murine and feline pneumonitis from one another. Although establishment of a given virus as a member of the group is readily accomplished by the complement-fixation test, identification of the individual virus falls into the realm of investigative research. However, the only rapid serologic diagnostic tool readily available to the clinician is the complement-fixation test, which he must interpret with care in conjunction with clinical manifestations.[131, 132]

Complement-fixing antibodies may appear in the serum of patients ill with psittacosis from four to eight days after the onset of symptoms. Complement fixation in dilution of 1:16 or greater is considered highly suggestive of psittacosis or psittacosis-like infection. However, a fourfold or greater rise in antibody titer during the course of an illness is most significant when the early and late serum samples are tested in the same experimental series. A serum titer of 1:8 or 1:16 during acute illness, which drops during convalescence, is a nonspecific reaction because in psittacosis the titer rises during convalescence and usually persists for many months and even years. This is particularly true with serums of patients infected with the virus of acute lymphogranuloma venereum, which occasionally yield significantly high complement-fixation titers in the presence of psittacosis virus but which fade during convalescence. Serum from patients with positive Wassermann reactions may react strongly with psittacosis antigen when they are simultaneously infected in a latent state with the virus of lymphogranuloma venereum.[133] Persons constantly exposed to psittacosis virus, such as aviary owners, pet-shop employees and pigeon breeders, as a rule show complement-fixing antibodies in their serums in titers varying from 1:8 to 1:32.[131] The persistence of a high titer of complement-fixing antibodies in the serum of a recovered patient at the end of twelve months suggests latent infection with survival of the virus in the tissues. Cold agglutinins as a rule are not demonstrable in the blood of patients with psittacosis.

With the discovery of potent antigens,[134, 135] the complement-fixation test for lymphogranuloma venereum has come to be regarded as a more sensitive diagnostic tool than the intradermal Frei test.[136] The complement-fixation test becomes positive before the intradermal test and becomes negative after the intradermal test in the event of successful therapy or spontaneous cure. Thus, the complement-fixation test may be useful in the evaluation of clinical cures. It must be remembered that skin-test materials are antigenic and stimulate the production of antibodies that may confuse the serologic picture by causing false-positive reactions. Hence, tests for dermal hypersensitivity should not be done if the complement-fixation test is going to be used in diagnosis. Furthermore, like the complement-fixation test, the intradermal test is psittacosis-lymphogranuloma group reactive,[137, 138] and the results of both positive tests must be evaluated

in the light of the clinical findings and history of the patient.

It is not possible to set definite levels that indicate definite prior or continuing infection; however, dilutions of 1:6 or above are significant. Demonstration of a rise in titer during the course of illness is more significant. There are nonspecific reactions in early syphilis, in which both specific lymphogranuloma venereum and control yolk-sac antigens give fixation. Therefore, it is necessary to use a boiled phenolized antigen[139] to avoid most, if not all, of these nonspecific reactions, and it is also wise to run a serologic test for syphilis as a control.

Tests for Rickettsial Infections

The rickettsias are micro-organisms intermediate in characteristics between bacteria and viruses.

Table 3. *Usual Weil-Felix Agglutination Reactions Observed in Rickettsial Disease.**

Disease	Reaction to *Proteus OX-19*	Reaction to *Proteus OX-2*	Reaction to *Proteus OX-K*
Epidemic typhus	++++	+	0
Endemic typhus	++++	+	0
Scrub typhus	0	0	++++
Q Fever	0	0	0
Rocky mountain spotted fever	++++	+	0
	+	++++	0

*Modified from Plotz.[144]

On the basis of clinical features, epidemiologic aspects and serologic and immunologic characteristics, human infections with these organisms have been divided into the following groups: typhus group (classic epidemic or louse-borne typhus, probably including Brill's disease, and murine or flea-borne typhus); spotted-fever group (Rocky Mountain spotted fever, boutonneuse fever [Mediterranean area], Brazilian spotted fever, Tobia fever [Colombia], Choix or pinta fever [Mexico], Kenya fever, South African tick-bite fever, rickettsialpox, North Queensland tick typhus and possibly some of the tick-borne rickettsial diseases of India and Russia); scrub typhus (tsutsugamushi disease); Q fever; and trench fever. The development of suitable methods for obtaining appreciable quantities of rickettsial organisms and other recent advances have made serologic methods readily available for the specific diagnosis of these diseases.

Weil-Felix Test

The Weil–Felix test continues to be of considerable importance in the early presumptive diagnosis of many rickettsial diseases.[140] A slide[141, 142] and a test-tube[143] agglutination test are available; however, the latter is considered to be more accurate. The typical responses obtained with suspensions of *Proteus OX-19*, *OX-2* and *OX-K* organisms and convalescent serums from patients with more common rickettsial infections are given in Table 3, as modified by Plotz[144] from Felix.[140] Serums from patients with epidemic and murine typhus agglutinate *Proteus OX-19* organisms, those from patients with scrub typhus *Proteus OX-K* organisms, and those from patients with Q fever, none. Serums from patients with Rocky Mountain spotted fever may agglutinate *Proteus OX-19* in high and *Proteus OX-2* in low titers or vice versa or both relatively equally. Although titers of 1:160 or above are diagnostically significant, a rise in antibody titer, demonstrated in a series of two or more serums, is necessary for a presumptive diagnosis. Weil–Felix agglutinins appear in the blood five or six days after onset, reach a maximum by the third week and then decline to nondiagnostic levels in one to several months. Some patients with typhus or spotted fever do not develop *Proteus OX* agglutinins, particularly, those vaccinated but subsequently developing typhus.[145] The Weil–Felix test does not differentiate epidemic from murine typhus or, sometimes, the typhus group from the spotted-fever group. It is negative in rickettsialpox.

Complement-Fixation Test

With the development of methods for preparing materials rich in rickettsias,[146-148] the complement-fixation and agglutination tests have come to be more frequently employed in clinical diagnostic work. Specific complement-fixing antibodies are present in convalescent serums of patients with typhus-group, spotted-fever group and scrub-typhus infections; however, certain of these rickettsial agents have antigens that are closely related. For instance, epidemic and murine typhus have a common soluble antigen,[149-151] which makes differentiation difficult unless thoroughly washed rickettsial organisms are used as antigen.[152] These highly purified rickettsial antigens are relatively expensive, whereas the less thoroughly washed antigens are comparatively cheap. However, antibodies for a homologous agent are, as a rule, at a higher level than those for heterologous agents. Spotted-fever and boutonneuse-fever rickettsias also contain common soluble cross-fixing antigens,[153] which can be removed by repeated washings. Purified soluble antigens from spotted fever rickettsias have also been prepared that are highly specific and give little or no fixation with syphilitic human serums.[154]

Complement-fixing antibodies may be detected in the serums of patients by the end of the first or the beginning of the second week after onset, reach a peak by the first two or three weeks of convalescence and then fall slowly over a period of months to low levels, which may persist for years. Occasionally, titers may fall to 0 a few weeks after the end of the disease. In general, a titer of 1:10 is significant in complement-fixation tests in which

washed rickettsial antigens are used; however, at some time during convalescence titers well above 1:200 are usually obtained. It is essential to demonstrate a rise in specific antibodies during convalescence as in other serologic tests. Serums of persons previously injected with epidemic typhus-fever vaccine generally show a complement-fixation titer with epidemic antigen of 1:4 to 1:32. Furthermore, when such vaccinated persons become infected with either the homologous or the heterologous typhus organisms, there is a prompt rise in both epidemic and murine typhus antibodies, and the amount of crossing may preclude differentiation between the two diseases.[143, 155, 156]

Agglutination Test

Rickettsial agglutination tests are satisfactory for diagnostic purposes in epidemic and murine typhus and in Q fever. However, technical difficulties preventing the preparation of rich, purified suspensions of rickettsias keep the test from being used more extensively with the spotted-fever group and scrub typhus. A slide test is available,[141, 157, 158] but the test-tube method is preferred generally.[152]

Agglutinins appear and persist in the serums of persons ill with epidemic or murine typhus approximately at the same time as the complement-fixing antibodies. However, in Q fever agglutinins begin to appear by the end of the second week and are present in 90 per cent of patients by the end of the fourth week.[159] Demonstration of the appearance of antibodies or their increase in titer during convalescence is essential. However, rickettsial agglutination titers above 1:25 to 1:40 are probably significant in epidemic and murine typhus, whereas titers greater than 1:5 are considered diagnostic for Q fever.

Tests for Parasitic Infections

The formation of specific antibodies against parasitic antigens in the host has been used for diagnostic purposes with variable results. Parasites whose by-products have been diffused through the body of the host are best adapted to serologic diagnosis. The complement-fixation test has met with some success in echinococcal infections, schistosomiasis, amebiasis and trichinosis. The precipitin test has also been used with some success in trichinosis and echinococcosis. Some consistent results have been obtained in kala-azar with nonspecific flocculation tests that depend upon the high euglobulin content of the blood serum. Demonstration of the parasite, however, is still the most reliable laboratory evidence available for the confirmation of a diagnosis.

The tests most widely or frequently used in this country have been those for amebiasis and trichinosis. But, in spite of improvement in technical details and the provision of more satisfactory antigens, it is difficult to evaluate the specificity and sensitivity of the complement-fixation tests for these diseases from the variability of results in published reports. The precipitin test for trichinosis is considered generally specific by most investigators. It becomes positive usually during the fourth week, reaching high titers subsequently. Although nonspecific reactions do occur, a positive titer of 1:2500 dilution of antigen or a rising titer on serially taken serum samples is specific in most trichinous patients.[160] The value of this test is minimized by many investigators in that it becomes positive late in the course of the pathologic process and persists for a year or two after infection.[161]

Toxoplasmosis

Serologic methods available for confirming clinical impressions of toxoplasmosis are tests for toxoplasma-neutralizing antibody and complement fixation. The rabbit neutralization test[162, 163] consists of demonstrating neutralizing antibodies by their inhibiting effects in toxoplasma-serum mixtures on the development of papulonecrotic cutaneous lesions in rabbits at the sites of intradermal injection with various dilutions of toxoplasma. This has proved to be a useful test but with many disadvantages.[164, 165] Recently, a new in vitro test has been introduced that is based on the principle that toxoplasma incubated with immune serum loses its ability to stain with methylene blue and other vital stains.[166] This test correlates favorably with the skin and rabbit neutralization tests and is recommended for routine diagnostic studies since it is easier and quicker to perform.[167] The complement-fixation test, as first described by Warren and Sabin,[168] has been recently improved[169] and found to be more sensitive. However, although present studies hold promise for reliable and efficient serologic tests, attempts to base a diagnosis on one or another of these tests without other corroborative evidence are premature in the present state of knowledge of this disease.

Tests for Mycotic Infections

The diagnosis of mycotic infections rests on one or both of two laboratory procedures — namely, the actual demonstration of the causative fungus in tissue or exudate and its isolation in pure culture with specific identification. Agglutinins, precipitins and complement-fixing antibodies have been sought for many years in human mycoses and in experimentally infected animals. However, the accumulated evidence seems to indicate that these serologic methods have a very limited usefulness in the practical diagnosis of mycoses. Complement-fixing antibodies can be demonstrated in blastomycosis and coccidioidomycosis with a rise in titer indicating generalization of the infection and a poor prognosis. In general, serologic methods of diagnosis can be considered only as uncertain adjuncts to the direct demonstration of pathogenic fungi.

* * *

Serologic tests for all types of infection discussed are summarized in Table 4.

TABLE 4. *Serologic Tests for Infectious Diseases.*

INFECTION	SEROLOGIC PROCEDURES	BLOOD SERUM ANTIBODIES AFTER ONSET		LOWER LIMITS OF SIGNIFICANT RISES IN TITER*	REMARKS
		APPEARANCE	MAXIMUM		
Bacteria:					
Typhoid and paratyphoid fever	Agglutination test for "O" antigen Agglutination test for "H" antigen Agglutination test for "Vi" antigen	3rd–7th day	16th–22nd day	1:80	"O" and "H" titer of 1:80 or above signifies infection unless patient vaccinated recently. "O" titer of 1:80 or above with little to no "H" observed in 14 per cent of patients but most commonly in infections with organisms antigenically related to *E. typhosa*. "H" titer of 1:80 or above with little to no "O" signifies carrier (70-80 per cent) or recently vaccinated person and is occasionally indicative of past infection with no carrier state. "Vi" agglutinations present in 80-90 per cent of carriers and occasionally after vaccination — not necessary for diagnosis of acute cases
Tularemia	Agglutination test	1st or 2nd wk.	4th or 5th wk.	1:80	Vaccination yields titers of 1:10-1:160 for 9 to 11 mo. Cross-agglutination between *P. tularensis* and brucella; antibody titer higher with homologous organism.
Brucellosis or undulant fever	Agglutination test	1st or 2nd wk.	Variable	1:80–1:320	Cross-agglutination with *P. tularensis* and *V. cholerae*. Previous infection or vaccination with latter may result in agglutinins against brucella in low titer. Previous vaccine therapy or skin testing may yield positive test since materials used are antigenic. Tests unreliable in chronic infections. Test may be negative in active infection because of prozone phenomenon or "blocking" antibodies.
Rickettsias:					
Typhus (epidemic and murine)	Weil–Felix agglutination test with *Proteus OX-19*	5th–8th day	3rd week	1:160	Cross-reactions exist between murine and epidemic typhus, but titer is higher with antigen of infecting organism. Complement-fixation titers of 1:4-1:32 result frequently from vaccination with epidemic typhus. Titers not increased by febrile illnesses of nontyphus etiology.
	Agglutination test	5th–8th day	2nd–3rd wk.	1:25-1:40	
	Complement fixation	5th–8th day	2nd–3rd wk.	1:10	
Q fever	Agglutination test	9th–14th day	3rd–4th wk.	1:8	No Weil–Felix agglutination reaction. Tests highly specific. Serums with cold agglutinins do not react with Q fever antigens.
	Complement fixation	7th–13th day	3rd wk.	1:20	
Rocky Mountain spotted fever	Weil–Felix agglutination test and *Proteus OX-19* and *Ox-2*	2nd wk.	3rd–4th wk.	1:320	In Weil–Felix reaction, positive serums may agglutinate *OX-19* in higher or lower dilutions than *OX-2* or equally as high
	Agglutination test	2nd wk.	3rd–4th wk.	1:25-1:40	
	Complement fixation	2nd wk.	3rd–4th wk.	1:10	
Rickettsialpox	Complement fixation	2nd wk.	3rd–4th wk.	1:10	No Weil–Felix reaction. Related to Rocky Mountain spotted fever, giving cross-complement fixation
Scrub typhus	Weil–Felix agglutination test with *Proteus OX-K*	2nd wk.	3rd–4th wk.	1:160	Leptospirosis may give rise to *OX-K* agglutinins similar to scrub typhus.
	Complement fixation	2nd wk.	3rd–4th wk.	1:10	
Viruses:					
Meningoencephalitis:					
Eastern equine	Neutralization	1st wk.	2nd–3rd wk.	Neutralization index, 50	Time of appearance and wane of neutralizing antibodies and complement-fixing antibodies differ; hence, both tests should be performed.
Western equine	Complement fixation	2nd–3rd wk.	7th–8th wk.	1:8-1:64	
St. Louis	Neutralization	2nd–3rd wk.	4 mo.	Neutralization index, 50	Serologic crossing with Japanese B and West Nile may occur, but homologous reaction stronger than heterologous
	Complement fixation	1st–2nd wk.	3rd–4th wk.	1:8-1:64	
Japanese B	Neutralization	3rd–4th wk.	4 mo.	Neutralization index, 50	
	Complement fixation	1st–2nd wk.	3rd–4th wk.	1:8-1:64	
Lymphocytic Choriomeningitis	Neutralization	6th–10th wk.	4 mo. or more	Neutralization index, 50	
	Complement fixation	1st–2nd wk.	2nd–3rd wk.	1:8-1:64	
Infectious mononucleosis	Heterophil-antibody agglutination	1st wk.	2nd–3rd wk.	1:32	Agglutinins may be in normal serum to titer of 1:160 and in serum of person with serum sickness to titer of 1:20,480. Both types of agglutinins removed by adsorption with guinea-pig kidney. After horse serum injection heterophil antibodies may persist 1 yr. or more. Test positive in 50 to 80 per cent of cases.

TABLE 4 (*Concluded*).

Influenza	Hemagglutination inhibition	1st wk.	2nd-3rd wk.	Fourfold rise	Vaccination gives rise in titer similar to natural infection. To be suspected when antibodies to both types A and B show significant rise in complement-fixation test. Titers of normal serums cover wide range including very high levels. Failure to demonstrate rise in titer may be due to late collection of convalescent specimen, high initial antibody level or variations in specificity of response. By 8 to 12 mo. after onset titer is at or almost at preinfection level.
	Complement fixation	1st wk.	2nd-3rd wk.	Fourfold rise	
Mumps	Complement fixation	6 days	21 days	1:64	Complement-fixation test is preferred since normal serums frequently exhibit considerable nonspecific hemagglutination inhibition. Complement-fixation titers up to 1:6 in final dilution usually denote previous infection. Titer of 1:64 rarely exceeded in serum of normal persons unless infected within preceding year. Skin-testing antigen stimulates production or increase of antibody and hence should be deferred.
	Hemagglutination inhibition	6 days	21 days	Fourfold increase	
Primary atypical pneumonia	Cold hemagglutinin test	1st-2nd wk.	3rd-4th wk.	1:128-1:1024	Cold hemagglutinins found in mumps orchitis, hemolytic anemias, certain liver diseases and certain peripheral vascular diseases and in low titers in various common respiratory diseases
	Streptococcus MG Agglutination test	2nd-3rd wk.	4th-5th wk.	1:20	*Str. MG* agglutination demonstrated only in this disease. No correlation between 2 tests; fair correlation between severity and development of positive titers in both tests.
Psittacosis	Complement fixation	4th-8th day	4th-5th wk.	1:16	Cross-complement fixation with lymphogranuloma venereum. No cold agglutinins demonstrable. Recovered patient with high titer at end of 12 mo. usually signifies latent infection with survival of virus in tissues.
Lymphogranuloma venereum	Complement fixation	Approximately 1 mo.	Unknown	1:4	Probably positive as long as virus is in host
Spirochetes:					
Leptospirosis	Agglutination test	7 days	4th-7th wk.	1:1000	Titers of 1:100 or less early in course of disease must be re-examined after 5 days. Agglutinins from previous infection may persist for years.
Syphilis	Complement fixation	6th-8th wk.	Secondary stage	None	Height of single titer not related to degree of infection or degree of host's immunity and has no bearing on prognosis. Rising serial titers connote active progression of disease; falling serial titers, subsidence. Similar sequence can be manifested in biologic false-positive reactions; hence, lacking corroborative evidence, tests for detecting false-positive reactions should be applied. Fluctuating serial titers without specific therapy connote false-positive reaction. False-positive titers usually low in adults, occasionally high in children with febrile illness. Serial reagin in titers useful in diagnosis of dark-field-negative primary and congenital syphilis, recognition of relapse, differentiation of seroresistance from serorelapse, determination of response to specific therapy, detection of prozone phenomenon and detection of biologic false-positive reactions.
	Precipitin				

*No significant diagnostic titer limits can be set for serologic tests. Definite diagnosis can be made only when rise in antibody titer can be demonstrated between acute and convalescent stages of disease, clinical signs and symptoms are suggestive and there is no laboratory or clinical evidence of other diseases. In viral infections fourfold rise in antibody titer during course of illness has been generally accepted as significant.

REFERENCES

62. Ayres, J. C. and Feemster, R. F. Public-health aspects of virus encephalitides. *New Eng. J. Med.* **240**:966-975, 1949.
63. Hammon, W. M. Encephalitides of virus origin with special reference to those of North America. *Clinics* **4**:485-503, 1945.
64. Olitsky, P. K., and Casals, J. Neutralization tests for diagnosis of human viral encephalitides. *J. A. M. A.* **134**:1224-1228, 1947.
65. Casals, J., and Palacios, R. Complement-fixation test in diagnosis of virus infections of the central nervous system. *J. Exper. Med.* 74:409-426, 1941.
66. Casals, J. Technique and practical applications of complement-fixation test for the diagnosis of infection with encephalitis viruses. *J. Bact.* **50**:1-5, 1945.
67. *Idem.* Heated, avirulent antigens for complement-fixation tests with certain encephalitis viruses. *Science* **102**:618, 1945.
68. Sabin, A. B. Epidemic encephalitis in military personnel: isolation of Japanese B virus on Okinawa in 1945, serologic diagnosis, clinical manifestations, epidemiologic aspects and use of mouse brain vaccine. *J. A. M. A.* **133**:281-293, 1947.
69. Howitt, B. F. Complement fixation reaction in experimental equine encephalomyelitis, lymphocytic choriomeningitis and St. Louis type of encephalitis. *J. Immunol.* **33**:235-250, 1937.

70. Casals, J. Immunological relationships among central nervous system viruses. *J. Exper. Med.* **79**:341-359, 1944.
71. Casals, J., and Olitsky, P. K. Enduring immunity following vaccination of mice with formalin-inactivated virus of Russian spring-summer (Far Eastern, tick-borne) encephalitis: correlation with serum-neutralizing and complement-fixing antibodies. *J. Exper. Med.* **82**:431-443, 1945.
72. Smadel, J. E., Baird, R. D., and Wall, M. J. Complement-fixation in infections with virus of lymphocytic choriomeningitis. *Proc. Soc. Exper. Biol. & Med.* **40**:71-73, 1939.
73. Casals, J. Diagnosis of epidemic encephalitis by complement-fixation tests. *Am. J. Pub. Health* **31**:1281-1284, 1941.
74. Howitt, B. F. Complement-fixation test with human sera against viruses of St. Louis encephalitis and equine encephalomyelitis. *J. Immunol.* **47**:293-302, 1943.
75. Milzer, A. Neurotropic virus infections in Chicago, 1931-1941. Nine cases of lymphocytic choriomeningitis. *Proc. Soc. Exper. Biol. & Med.* **54**:279-282, 1943.
76. Hodes, H. L., Thomas, L., and Peck, J. L. Cause of outbreak of encephalitis established by means of complement-fixation tests. *Proc. Soc Exper. Biol. & Med.* **60**:220-225, 1945.
77. Hammon, W. McD. Encephalitis. In *Diagnostic Procedures for Virus and Rickettsial Diseases.* 347 pp. New York: American Public Health Association, 1948. Pp. 187-217.
78. Friedemann, U. Über heterophile Normalamboceptoren: ein Beitrag zur Lehre von der Entstehung der normalen Antikörper. *Biochem. Ztschr.* 80:333-356, 1917.
79. Taniguchi, T. Studies on heterophile antigen and antibody. *J. Path. & Bact.* **25**:77-93, 1922.
80. Bailey, G. H., and Raffel, S. Hemolytic antibodies for sheep and ox erythrocytes in infectious mononucleosis. *J. Clin. Investigation* **14**:228-244, 1935.
81. Stuart, C. A. Heterophile antibodies in infectious mononucleosis. *Proc. Soc. Exper. Biol. & Med.* **32**:861-863, 1935.
82. Stuart, C. A., Fulton, M., Ash, R., and Gregory, K. Relations between certain heterophile antibodies and antigens. *J. Infect. Dis.* **59**:65-71, 1936.
83. Davidsohn, I. Heterophile antibodies in serum sickness. *J. Immunol.* **16**:259-273, 1929.
84. Hirst, G. K. In vivo titrations of influenza virus and of neutralizing antibodies in chick embryos. *J. Immunol.* **45**:285-292, 1942.
85. Burnet, F. M., and Beveridge, W. I. B. Titration of antibody against influenza viruses by allantoic inoculation of developing chick embryo. *Australian J. Exper. Biol. & Med. Sc.* **21**:71-77, 1943.
86. Smith, W. Complement-fixation reaction in influenza. *Lancet* **2**: 1256-1259, 1936.
87. Friedewald, W. F. Immunological response to influenza virus infection as measured by complement-fixation test: relation of complement-fixing antigen to virus particle. *J. Exper. Med.* **78**:347-366, 1943.
88. Salk, J. E. Simplified procedure for titrating hemagglutinating capacity of influenza-virus and corresponding antibody. *J. Immunol.* **49**:87-98, 1944.
89. Hirst, G. K., and Pickels, E. G. Method for titration of influenza hemagglutinins and influenza antibodies with aid of photoelectric densitometer. *J. Immunol.* **45**:273-283, 1942.
90. Miller, G. L., and Stanley, W. M. Quantitative aspects of red blood cell agglutination test for influenza virus. *J. Exper. Med.* **79**: 185-195, 1944.
91. Francis, T., Jr. New type of virus from epidemic influenza. *Science* **92**:405-408, 1940.
92. Magill, T. P. Virus from cases of influenza-like upper-respiratory infection. *Proc. Soc. Exper. Biol. & Med.* **45**:162-164, 1940.
93. Henle, W., Henle, G., Hampil, B., Maxis, E. P., and Stokes, J., Jr. Experiments on vaccination of human beings against epidemic influenza. *J. Immunol.* **53**:75-93, 1946.
94. Enders, J. F., and Cohen, S. Detection of antibody by complement-fixation in sera of man and monkey convalescent from mumps. *Proc. Soc. Exper. Biol. & Med.* **50**:180-184, 1942.
95. Enders, J. F., Kane, L. W., Cohen, S., and Levens, J. H. Immunity in mumps. I. Experiments with monkeys (*Macacus mulatta*). Development of complement-fixing antibody following infection and experiments on immunization by means of inactivated virus and convalescent human serum. *J. Exper. Med.* **81**:93-117, 1945.
96. Habel, K. Cultivation of mumps virus in developing chick embryo and its application to studies of immunity to mumps in man. *Pub. Health Rep.* **60**:201-212, 1945.
97. Beveridge, W. I. B., Lind, P. E., and Anderson, S. G. Mumps. I. Isolation and cultivation of virus in chick embryo. *Australian J. Exper. Biol. & Med. Sc.* **24**:15-19, 1946.
98. Levens, J. H., and Enders, J. F. Hemoagglutinative properties of amniotic fluid from embryonated eggs infected with mumps virus. *Science* **102**:117-120, 1945.
99. Maris, E. P., Enders, J. F., Stokes, J., Jr., and Kane, L. W. Immunity in mumps. IV. Correlation of presence of complement-fixing antibody and resistance to mumps in human beings. *J. Exper. Med.* **84**:323-339, 1946.
100. Kane, L. W., and Enders, J. F. Immunity in mumps. III. Complement-fixation test as aid in diagnosis of mumps meningoencephalitis. *J. Exper. Med.* **81**:137-150, 1945.
101. Enders, J. F., Kane, L. W., Maris, E. P., and Stokes, J., Jr. Immunity in mumps. V. Correlation of presence of dermal hypersensitivity and resistance to mumps. *J. Exper. Med.* **84**:341-364, 1946.
102. Horsfall, F. L., Jr. Primary atypical pneumonia. *New York State J. Med.* **46**:1810-1814, 1946.
103. Turner, J. C., Nisnewitz, S., Jackson, E. B., and Berney, R. Relation of cold agglutinins to atypical pneumonia. *Lancet* 1:765-769, 1943.
104. Commission on Acute Respiratory Diseases. Cold hemagglutinins in primary atypical pneumonia and other respiratory infections. *Am. J. M. Sc.* **208**:742-750, 1944.
105. Finland, M., et al. Cold agglutinins. I. Occurrence of cold isohemagglutinins in various conditions. *J. Clin. Investigation* **24**: 451-457, 1945.
106. Young, L. E. Clinical significance of cold hemagglutinins. *Am. J. M. Sc.* **211**:23-39, 1946.
107. Favour, C. B. Autohemagglutinins — "cold agglutinins." *J. Clin. Investigation* **23**:891-897, 1944.
108. Commission on Acute Respiratory Diseases. Transmission of primary atypical pneumonia to human volunteers. IV. Laboratory studies. *Bull. Johns Hopkins Hosp.* **79**:153-167, 1946.
109. Thomas, L., Mirick, G. S., Curnen, E. C., Ziegler, J. E., and Horsfall, F. L., Jr. Serological reactions with indifferent streptococcus in primary atypical pneumonia. *Science* **98**:566-568, 1943.
110. *Idem.* Studies on primary atypical pneumonia. II. Observations concerning relationship of non-hemolytic streptococcus to disease. *J. Clin. Investigation* **24**:227-240, 1945.
111. Curnen, E. C. Virus pneumonia. *J. Pediat.* **29**:309-315, 1946.
112. Meiklejohn, G., and Hanford, V. L. Agglutination tests with Streptococcus no. 344 in primary atypical pneumonia. *Proc. Soc. Exper. Biol. & Med.* **57**:356-358, 1944.
113. Eaton, M. D. Serological differentiation of primary atypical pneumonia from virus pneumonia of psittacosis group. *Proc. Soc. Exper. Biol. & Med.* **60**:231-235, 1945.
114. Finland, M., Samper, B. A., and Barnes, M. W. Cold agglutinins. VI. Agglutinins for indifferent streptococcus in primary atypical pneumonia and in other conditions and their relationship to cold isohemagglutinins. *J. Clin. Investigation* **24**:497-502, 1945.
115. Commission on Acute Respiratory Diseases. Laboratory aids in diagnosis of primary atypical pneumonia. *Bull. U. S. Army M. Dept.* **5**:10-12, 1946.
116. Florman, A. L., and Weiss, A. B. Serologic reactions in primary atypical pneumonia. *J. Lab. & Clin. Med.* **30**:902-910, 1945.
117. Bedson, S. P., and Bland, J. O. W. Morphological study of psittacosis virus, with description of developmental cycle. *Brit. J. Exper. Path.* **13**:461-466, 1932.
118. Meyer, K. F., Eddie, B., and Yanamura, H. Y. Ornithosis (psittacosis) in pigeons and its relation to human pneumonitis. *Proc. Soc. Exper. Biol. & Med.* **49**:609-615, 1942.
119. Meyer, K. F., and Eddie, B. Spontaneous ornithosis (psittacosis) in chickens cause of human infection. *Proc. Soc. Exper. Biol. & Med.* **49**:522-525, 1942.
120. Francis, T., Jr., and Magill, T. P. Unidentified virus producing acute meningitis and pneumonitis in experimental animals. *J. Exper. Med.* **68**:147-160, 1938.
121. Eaton, M. D., Beck, M. D., and Pearson, H. E. Virus from cases of atypical pneumonia: relation to viruses of meningo-pneumonitis and psittacosis. *J. Exper. Med.* **73**:641-654, 1941.
122. Olson, B. J., and Larson, C. L. Epidemic of severe pneumonitis in bayou region of Louisiana. V. Etiology. *Pub. Health Rep.* **60**: 1488-1503, 1945.
123. Zichis, J., and Shaughnessy, H. J. Isolation of apparently new virus from two fatal pneumonia cases. *Science* **102**:301, 1945.
124. Gönnert, R. Die Bronchopneumonie, eine neue Viruskrankheit der Maus. *Zentralbl. f. Bakt.* (Abt. 1) **147**:161-174, 1941.
125. Nigg, C., and Eaton, M. D. Isolation from normal mice of pneumotropic virus which forms elementary bodies. *J. Exper. Med.* **79**: 497-510, 1944.
126. Deburgh, P., Jackson, A. V., and Williams, S. E. Spontaneous infection of laboratory mice with psittacosis-like organism. *Australian J. Exper. Biol. & M. Sc.* **23**:107-110, 1945.
127. Baker, J. A. Virus causing pneumonia in cats and producing elementary bodies. *J. Exper. Med.* **79**:159-172, 1944.
128. Levaditi, C., Ravaut, P., Lépine, P., and Schoen, R. Étude étiologique et pathogénique de la maladie de Nicolas et Favre (lymphogranulomatose inguinale subaiguë, ulcère vénérien adénogène, poradénolymphite). *Ann. Inst. Pasteur* **48**:27-88, 1932.
129. Findlay, G. M. Experiments on transmission of virus of climatic bubo (lymphogranuloma inguinale) to animals. *Tr. Roy. Soc. Trop. Med. & Hyg.* **27**:35-66, 1933.
130. Moshkovskii, S. D. Tsitatroprie vozbyditeli infektsii i mesto rikettsii v sisteme snlamydozoa. *Uspekhi souremeunoi biologii* **19**: 1-44, 1945.
131. Meyer, K. F. Ecology of psittacosis and ornithosis. *Medicine* **21**: 175-206, 1942.
132. Smadel, J. E., Wertman, K., and Regan, R. L. Yolk sac complement-fixation antigen for use in psittacosis-lymphogranuloma venereum group of diseases. *Proc. Soc. Exper. Biol. & Med.* **54**: 70-74, 1943.
133. Rake, G., Eaton, M. D., and Shaffer, M. F. Similarities and possible relationships among viruses of psittacosis, meningopneumonitis, and lymphogranuloma venereum. *Proc. Soc. Exper. Biol. & Med.* **48**:528-531, 1941.
134. Rake, G., McKee, C. M., and Shaffer, M. F. Agent of lymphogranuloma venereum in yolk-sac of developing chick embryo. *Proc. Soc. Exper. Biol. & Med.* **43**:332-334, 1940.
135. Shaffer, M. F., Rake, G., and McKee, C. M. Agent of lymphogranuloma venereum in lungs of mice. *Proc. Soc. Exper. Biol. & Med.* **44**:408-410, 1940.
136. Rake, G., Shaffer, M. F., Grace, A. W., McKee, C. M., and Jones, H. P. New aids in diagnosis of lymphogranuloma venereum. *Am. J. Syph., Gonor. & Ven. Dis.* **25**:687-698, 1941.

137. Levine, S., Holder, E. C., and Bullowa, J. G. M. Complement fixation for lymphogranuloma venereum and for psittacosis with Frei reactions among pneumonia patients. *J. Immunol.* **46**: 183-188, 1943.
138. Kilham, L. Skin-test antigen common to five viruses of psittacosis-lymphogranuloma group. *J. Immunol.* **60**:157-165, 1948.
139. Bowser, B. M., and Nigg, C. Studies on lymphogranuloma venereum complement-fixing antigens. II. Serological studies with boiled phenolized antigens. *J. Immunol.* **53**:269-275, 1946.
140. Felix, A. Serological types of typhus virus and corresponding types of Proteus. *Tr. Roy. Soc. Trop. Med. & Hyg.* **27**:147-172, 1933.
141. Castaneda, M. R. Clinical and experimental aspects of exanthematous typhus in tropical regions of America; aids to diagnosis. *Puerto Rico J. Pub. Health & Trop. Med.* **18**:165-174, 1942.
142. Welch, H., and Bengston, I. A. Typhus fevers and other rickettsial infections. In *Diagnostic Procedures and Reagents*. Second edition. 549 pp. New York: American Public Health Association, 1945. Pp. 232-246.
143. Plotz, H. Rickettsiae. In *Laboratory Methods of the United States Army*. Edited by J. S. Simmons and C. J. Gentzkow. Fifth edition. 823 pp. Philadelphia: Lea & Febiger, 1944. P. 575.
144. *Idem.* Interpretation of Weil-Felix agglutination test in Rocky Mountain spotted fever. *J. Lab. & Clin. Med.* **31**:982-986, 1946.
145. Zarafonetis, C. J. D., Ecke, R. S., Yeomans, A., Murray, A. S., and Snyder, J. C. Serologic studies in typhus-vaccinated individuals. III. Weil-Felix and complement-fixation findings in epidemic typhus fever occurring in vaccinated. *J. Immunol.* **53**:15-30, 1946.
146. Cox, H. R. Use of yolk sac of developing chick embryo as medium for growing Rickettsiae of Rocky Mountain spotted fever and typhus groups. *Pub. Health Rep.* **53**:2241-2247, 1938.
147. Castaneda, M. R. Experimental pneumonia produced by typhus Rickettsiae. *Am. J. Path.* **15**:467-476, 1939.
148. Zinsser, H., Fitzpatrick, F., and Wei, H. Study of Rickettsiae grown on agar tissue cultures. *J. Exper. Med.* **69**:179-190, 1939.
149. Topping, N. H., Bengston, I. A., and Shear, M. J. *Studies of Typhus Fever.* 110 pp. Sections III and IV. National Institute of Health Bulletin No. 183. Washington, D. C.: Government Printing Office, 1945. Pp. 13-24.
150. Craigie, J., Watson, D. W., Clark, E. M., and Malcolmson, M. E. Serological relationship of rickettsiae of epidemic and murine typhus. *Canad. J. Research*, Sect. E. **24**:84-103, 1946.
151. Fulton, F., and Begg, A. M. V. Antigenic structure of typhus rickettsiae. In *Chemotherapeutic and Other Studies of Typhus.* Medical Research Council, Special Report Series No. 255. 246 pp. London: His Majesty's Stationery Office, 1946. Pp. 163-191.
152. Plotz, H., Bennett, B. L., Worthman, K., Snyder, M. J., and Gould, R. L. Serological pattern in typhus fever. I. Epidemic. *Am. J. Hyg.* **47**:150-165, 1948.
153. Plotz, H., Reagan, R. L., and Wertman, K. Differentiation between fièvre boutonneuse and Rocky Mountain spotted fever by means of complement fixation. *Proc. Soc. Exper. Biol. & Med.* **55**:173-176, 1944.
154. Van der Scheer, J., Bohnel, E., and Cox, H. R. Diagnostic antigens for epidemic typhus, murine typhus and Rocky Mountain spotted fever. *J. Immunol.* **56**:365-375, 1947.
155. Smadel, J. E. Complement-fixation and agglutination reaction in rickettsial diseases. In *Rickettsial Diseases of Man.* Edited by R. F. Moulton. 247 pp. Washington, D. C.: American Association for the Advancement of Science, 1948. Pp. 190-197.
156. Plotz, H., and Wertman, K. Modification of serological response to infection with murine typhus by previous immunization with epidemic typhus vaccine. *Proc. Soc. Exper. Biol. & Med.* **59**: 248-251, 1945.
157. Fitzpatrick, F. K. Studies on rickettsial agglutination in typhus. *J. Lab. & Clin. Med.* **30**:577-586, 1945.
158. Giroud, P., and Giroud, M. Agglutination des rickettsies, test de séro-protection et réaction d'hypersensibilité cutanée. *Bull. Soc. path. exot.* **37**:84-93, 1944.
159. Commission on Acute Respiratory Diseases. Identification and characteristics of Balkan grippe strain of *Rickettsia burneti*. *Am. J. Hyg.* **44**:110-122, 1946.
160. Dammin, G. J. Trichinosis: report of case, with demonstration of larva in arterial blood. *New Eng. J. Med.* **224**:357-360, 1941.
161. Augustine, D. L. Trichinosis and enterobiasis: their importance in New England. *New Eng. J. Med.* **226**:488-495, 1942.
162. Sabin, A. B., and Ruchman, I. Characteristics of toxoplasma neutralizing antibody. *Proc. Soc. Exper. Biol. & Med.* **51**:1-6, 1942.
163. Sabin, A. B. Toxoplasma neutralizing antibody in human beings and morbid conditions associated with it. *Proc. Soc. Exper. Biol. & Med.* **51**:6-10, 1942.
164. Heidelman, J. M. Evaluation of toxoplasma neutralization tests in cases of chorioretinitis. *Arch. Ophth.* **34**:28-39, 1945.
165. Frenkel, J. K. Dermal hypersensitivity to toxoplasma antigens (toxoplasmins). *Proc. Soc. Exper. Biol. & Med.* **68**:634-639, 1948.
166. Sabin, A. B., and Feldman, H. A. Dyes as microchemical indicators of new immunity phenomenon affecting protozoan parasite (toxoplasma). *Science* **108**:660-663, 1948.
167. Adams, F. H., Kabler, P., Cooney, M., and Adams, J. M. Diagnostic tests for toxoplasmosis. *Pediatrics* **4**:490-497, 1949.
168. Warren, J., and Sabin, A. B. Complement fixation reaction in toxoplasmic infection. *Proc. Soc. Exper. Biol. & Med.* **51**:11-14, 1942.
169. Warren, J., and Russ, S. B. Cultivation of toxoplasma in embryonated eggs: antigen derived from chorioallantoic membrane. *Proc. Soc. Exper. Biol. & Med.* **67**:85-89, 1948.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 36521

PRESENTATION OF CASE

A sixty-four-year-old man was admitted to the hospital with the complaint of swelling of the right eye and nasal discharge.

He had first noted some swelling of the right eye one year before entry. This was accompanied by some tearing but no pain, and he was able to carry on at work. Two weeks previous to admission he first noted some dimness of vision in the right eye, which was tender on pressure. There was a thin, watery discharge from the right nostril, and the right eye was tearing. His appetite, which had been poor for one year, became almost totally nonexistent, and he ate no solid food in this period. He had been losing weight for one year, with an estimated 20-pound weight loss in the month before entry. There was a vague history of attacks of diarrhea of one year's duration, and five days previous to admission he suddenly developed an explosive type of diarrhea. The stools were loose and watery, without blood or tarry material. Fecal incontinence was present from then until admission.

There were no serious illnesses or operations in the past. A chronic cough had been present for ten years. It had been somewhat more pronounced for the month prior to admission and had become productive of a greenish-yellow sputum, in which on some recent occasions there was questionable blood flecking. He had been hard of hearing all his life. There were no other constitutional symptoms.

Physical examination revealed an apathetic, listless, wasted man appearing somewhat older than the stated age. The right eye was prominent and showed increased orbital resistance. The conjunctiva was moderately injected, and the cornea lustrous,

with a few old scars. The pupil reacted poorly to light and accommodation. The lens, media, iris, disk and fundus were normal. There was limitation of downward gaze and external rotation; the other movements were normal. The vision was 20/40 on the right, and 20/200 on the left. The left pupil showed a sluggish reaction to light and accommodation, but otherwise this eye showed no abnormal findings. Located in relation to the right infraorbital margin was a palpable, painless, solid mass, which pushed the globe upward. Examination of the nasopharynx showed a smooth, brownish-red tumor hanging down from the right posterior choana. The neck veins were distended but non-pulsating. The veins in the arms remained filled

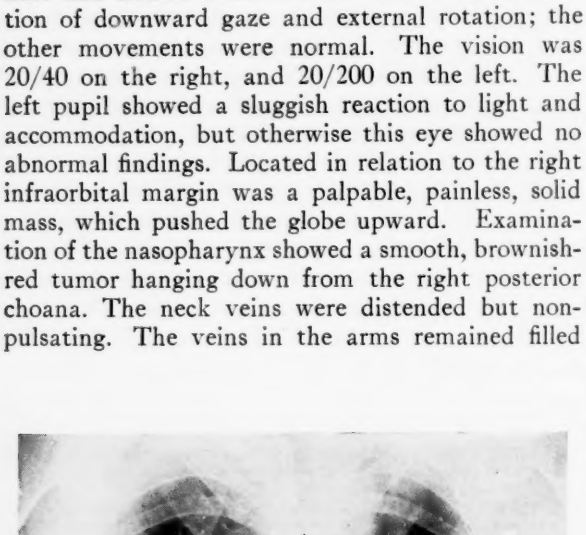

FIGURE 1.

with the arms raised one foot above the level of the heart. There were three hard lymph nodes palpable in the right anterior triangle of the neck. The chest was barrel shaped. There was diminution of breath sounds and vocal fremitus over the left upper chest, both anteriorly and posteriorly. There were no rales or rhonchi. The heart and abdomen were normal. On the left side of the scrotum there was a plaque of elevated, indurated, closely clumped nodules with an ulcerated center.

The temperature was 98.6°F., the pulse 90, and the respirations 30. The blood pressure was 100 systolic, 70 diastolic.

Urinalysis showed a specific gravity of 1.019 and a + test for albumin, and 15 to 20 white blood cells per high-power field in the sediment. Examination of the blood disclosed a hemoglobin of 11.5 gm. and a white-cell count of 64,000 on admission and of 52,000 on the following day, with 95 per cent neutrophils and 5 per cent lymphocytes. Fifteen per cent of the neutrophils were band forms. The nonprotein nitrogen was 70 mg., the total protein 6.3 gm., the fasting blood sugar 131 mg., the cholesterol 108 mg., the cholesterol esters 64 mg., and the alkaline phosphatase 7.4 Bodansky units per 100 cc.; the sodium was 135.7 milliequiv., the chloride 96 milliequiv., the potassium 3.6 milliequiv., and the carbon dioxide 30.4 milliequiv. per liter. The cephalin flocculation was ++ in twenty-four and forty-eight hours. An electrocardiogram showed third-degree heart block with an auricular rate of 60, a ventricular rate of 65 and occasional ventricular extrasystoles. A lumbar puncture resulted in clear spinal fluid with no cells and normal chemical findings. The pressure was not elevated.

X-ray films of the chest and fluoroscopy with a barium swallow showed the lung fields large and bright. The left-lung root was somewhat prominent. There was considerable generalized enlargement of the heart shadow, with posterior displacement of the esophagus by an enlarged left auricle. There was a ring density overlying the base of the aorta and a chain of calcified lymph nodes in the neck (Fig. 1). X-ray films of the skull and sinuses showed a mass in the right ethmoid and right side of the nose. This mass presented in the posterior choana. The roof of the right antrum and the inner rim of the right orbit were decalcified. A metastatic bone series was negative.

Biopsy of the lesion in the scrotum was reported as squamous-cell carcinoma, Grade II, and biopsy of the mass in the nasopharynx as acute and chronic inflammation.

Treatment consisted of penicillin, streptomycin, one intravenous injection of 1000 cc. of 5 per cent dextrose and terminally feeding by gastric tube. The patient continued to have diarrhea, with fecal incontinence, and later developed urinary incontinence. He became more drowsy and poorly responsive, was difficult to awaken, appeared to have memory lapses, and went progressively downhill, dying on the tenth hospital day.

During the entire hospital stay the temperature, pulse and respirations were within normal limits. On the sixth hospital day the nonprotein nitrogen was 100 mg. and the fasting blood sugar 104 mg. per 100 cc., and the white-cell count 54,000. Numerous urine examinations were negative for sugar and acetone.

DIFFERENTIAL DIAGNOSIS

DR. ALFRED KRANES*: After reading this history the first question I asked myself was why a medical man was asked to discuss a patient with a naso-

*Associate physician, Massachusetts General Hospital.

pharyngeal tumor. The only logical reason was that tumor must have been one local manifestation of some more widespread or generalized disease; otherwise the case would have been presented to an otorhinolaryngologist for discussion.

Whether that is a good or poor reason, I am going to omit from my discussion any consideration of local lesions in the nasopharynx, primarily because I know very little about them, and go on to a consideration of other diseases in which nasopharyngeal tumors may be a prominent manifestation. Fortunately, there are not many of these. Furthermore I shall not consider the possibility of an infectious process, despite the extraordinarily high white-cell count, because there seems to have been no acute infection and I cannot think of any chronic one that would behave in this manner.

Without much question this was a tumor, and the problem is to decide what type it was. If this was a metastatic lesion, the question also arises where the primary lesion could have been. We are told of one lesion of the scrotum, but a squamous-cell carcinoma of the scrotum would be unlikely to metastasize to the orbit or nasopharynx. I think that lesion was incidental. Most types of metastatic carcinoma are unlikely to involve this particular locality. The two sites that come to mind whenever bizarre metastases occur are the thyroid and the bronchus. Nothing was said here about the examination of the thyroid. I assume that it was normal, but that does not rule out a small carcinomatous nodule. A primary cancer of the bronchus is more difficult to exclude, particularly since the patient had a cough of some years' duration that had grown worse in recent months. Furthermore, there was a history of some questionable blood-flecked sputum, as well as an x-ray film showing some prominence of the left hilar area. There were, in addition, physical findings suggesting an obstruction of the superior mediastinum, since the neck veins were distended and there was some increase in the pressure of the arm veins.

This is probably a good time to look at the x-ray films, Dr. Wyman.

Dr. Stanley M. Wyman: I think the protocol very ably described the tumor in the right antrum and ethmoid, with the erosion of the roof of the antrum and the projection of the tumor back into the posterior choana. I do not agree with the description of the chest films (Fig. 1). These films were all taken with the patient in the supine position, and he was very sick.

Dr. Kranes: Is this the right or the left side?

Dr. Wyman: That is the question I asked myself when I looked at these films. The fluoroscopy showed the heart shadow to be just as it is here, and therefore I took this to be the patient's right and this his left. The aorta lies in normal position. The left hilus is definitely prominent and seems to have a discrete convexity suggesting enlarged lymph nodes. There is some fullness in the right superior mediastinum, with perhaps a little displacement of the esophagus.

Dr. Kranes: Where are the calcified lymph nodes?

Dr. Wyman: They are in the neck.

Dr. Kranes: I wonder if they are not the same nodes that were found clinically?

A Physician: Yes, that is where they were found clinically.

Dr. Wyman: The thing about this set of films that intrigues me is the abnormal prominence of the right side of the heart, which appears rather nobby and irregular. I cannot agree with the interpretation of a large left auricle.

Dr. Kranes: That is very helpful because it disturbed me considerably in reading the report. Do you think the heart is enlarged, or is that tumor?

Dr. Wyman: I think that is tumor, — metastases to the pericardium or even to the heart itself. I do not think the heart is large.

Dr. Kranes: I now have a completely different picture of this patient after having seen the films than I had when I read the description, and it alters my final decision. That makes some of what I was prepared to say rather obsolete, but I am going to say it anyway.

There is no collapse of any part of the lung?

Dr. Wyman: I cannot see it. I think as far as I can determine that the hilar shadows are approximately in normal position.

Dr. Kranes: I do not see how I can rule out primary bronchogenic carcinoma, after seeing the films. Do you agree?

Dr. Wyman: It did not occur to me. It is not the logical conclusion to draw, but one can never exclude it, of course.

Dr. Kranes: What dissuades me from a diagnosis of metastatic carcinoma is the fact that the local lesion in the eye was found a year before admission. Although it had grown somewhat there were no additional metastases that had become obvious in that year. It would be quite improbable for metastasis from a bronchogenic carcinoma to be present for a year without other metastases, particularly in the skeleton. The other objection is the manner of death. It would be difficult to postulate an abdomen full of bronchogenic carcinoma involving the kidneys and gut. There is, however, one possible although highly unlikely explanation. If one keeps in mind the propensity of bronchogenic carcinoma to metastasize to the adrenals, one might consider this terminal episode as acute adrenal failure — diarrhea, elevated nonprotein nitrogen, dehydration, hypotension and so forth. Since that is stretching things quite a bit, I shall discard that possibility.

There are several diseases of the bone marrow that might produce orbital and nasopharyngeal tumors. One, rather uncommon, is the chloroma

that occurs with myelogenous leukemia. With the white-cell count at the levels described here, one at least has to consider such a possibility. These greenish tumors most commonly involve the orbit and other areas of the nasopharynx, but they are much more likely to occur in young people. It is very unusual for one to occur at this age. Furthermore, chloroma is much more likely to occur in acute myelogenous leukemia than in a chronic one. I cannot make a diagnosis of chronic myelogenous leukemia in the absence of splenomegaly or any abnormal cells in the blood. Although only one smear was described, I assume others were probably similar.

There is one other bone-marrow disease that could produce this picture, and it is a diagnosis I should like very much to make — that is, multiple myeloma. One of the common sites of extramedullary myeloma formation is the nasopharynx. Outside the bone marrow it is probably the most common site. When I am presented with a nasopharyngeal tumor with renal insufficiency in the same patient, the first thing that occurs to me is multiple myeloma. There are a number of features in this story that it would explain very nicely. The only trouble is that there is nothing to support it. In order to make such a diagnosis one would at least like to have an elevated serum globulin, or some x-ray evidence of bone involvement, some Bence-Jones protein in the urine or possibly some plasma cells and so on. Although I am sure not all these things were looked for, and the disease can exist in the absence of some of them, I should not like to make the diagnosis on purely clinical grounds. I have never heard of a case of multiple myeloma with this degree of polymorphonuclear leukocytosis. When a leukemoid blood picture occurs the cells are usually plasma cells. Much as I should like to make that diagnosis, I see no way of supporting it.

The most likely possibility is some form of lymphoma. We know that occasionally involves the nasopharynx and orbit. The x-ray picture looks more like that seen in lymphoma than anything else I have considered. It is probable that there was infiltration of a good part of the gastrointestinal tract. One, of course, would like to have some confirmatory evidence, such as peripheral glandular involvement or some enlargement of the spleen, but the disease can exist in the absence of any one of these. Of the conditions I have considered malignant lymphoma best explains the clinical picture.

The patient obviously died with renal insufficiency, and the question arises, did the pathologic process present involve the kidneys? Not necessarily; I think probably not. This patient's uremia was very likely the result of marked fluid and electrolyte loss. Probably not much in the way of abnormal anatomic findings will be present in the kidneys. There may have been some lesion such as those recently described by Kulka et al.*—so-called vacuolar nephropathy, which is a form of proximal tubular nephrosis, large vacuoles being found in the tubules in patients dying of acute or chronic gastrointestinal diseases. How much of a role these lesions play in the development of renal insufficiency is questionable.

I shall conclude by making a diagnosis of probable lymphoma.

DR. WYMAN: Why is it not possible, Dr. Kranes, that the primary lesion was in the antrum and was ordinary carcinoma with metastases to the mediastinum, heart and pericardium?

DR. KRANES: I think that is perfectly possible. I just do not know enough about antral carcinoma and therefore I have not attempted to discuss it.

DR. RICHARD C. GOLDSMITH: Do you think tuberculosis is possible?

DR. KRANES: What sort of tuberculosis? Just caseous tuberculosis involving the nasopharynx? I do not think so.

CLINICAL DIAGNOSES

Carcinoma of nasopharynx, with mediastinal metastases.

Carcinoma of scrotum.

DR. KRANES'S DIAGNOSES

Malignant lymphoma, generalized with involvement of nasopharynx, mediastinum and gastrointestinal tract.

Squamous-cell carcinoma of scrotum.

ANATOMICAL DIAGNOSES

Carcinoma, bronchogenic, with extension to pericardium, myocardium and vena cava, and with metastases to antrum, orbital floor and nasopharynx.

Squamous-cell carcinoma of scrotum.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The striking finding when the chest was opened was the appearance of the heart and pericardium. Scattered over or involving almost the entire pericardium especially on the right side were large tumor nodules, some measuring as much as 6 cm. in diameter, that bulged from the surface of the heart and obliterated the entire pericardial cavity. When these were cut, a greenish-yellow, purulent material exuded as though from the center of an abscess. The mediastinal tumor perforated into the wall of the superior vena cava, formed a tumor thrombus and extended down into the right auricle. The bronchus to the superior lingular segment of the left lung and the lumen of the bronchus were involved with tumor. Also, we found tumor in the antrum on the right side extending down into the nasopharynx. The question arose at the time of autopsy whether the pri-

*Kulka, J. P., Pearson, C. M., and Robbins, S. L. Distinctive vacuolar nephropathy associated with intestinal disease. *Am. J. Path.* 26:349-378, 1950.

mary tumor was in the nasopharynx or in the lung. The tumor in the pericardium was continuous with the lesion in the left hilus so it was thought by some observers that the primary tumor was in the antrum, with metastases to the pericardium that, in turn, extended into the left lingular bronchus. The histology in both the antrum and chest showed a very undifferentiated carcinoma, but in addition there was definite differentiation to squamous cells in parts of the antral tumor. I am quite sure that the tumors in the antrum and pericardium were the same. My opinion is that the lung was the primary site although it is possible to explain the complete erosion of the bronchial wall by an extrinsic tumor forming a large mass within the bronchus. There were no other metastases outside the chest, which, as Dr. Kranes mentioned, is certainly a strong argument against a primary tumor in the bronchus that has been present over a year. However, I believe this was a primary tumor of bronchogenic origin with metastases to the nasal sinus.

DR. KRANES: As a solitary metastasis?

DR. CASTLEMAN: Yes; of course, all the mediastinal lymph nodes were involved.

DR. KRANES: What about the kidneys?

DR. CASTLEMAN: They showed nothing in particular so that you were correct in believing the renal condition was not caused by tumor. There was no tumor in the lymph nodes along the abdominal aorta that might have compressed the ureter. The bowel showed a mild enteritis, which may explain the diarrhea; we have no other explanation.

DR. JAMES H. CURRENS: Was there any tumor involving the interventricular septum to account for what I suppose was complete heart block?

DR. CASTLEMAN: There was a good deal of involvement of the myocardium, and I think part of it did involve the septum — an extension from the pericardium.

A PHYSICIAN: Can the mass in the scrotum be related?

DR. CASTLEMAN: The scrotum showed a very well differentiated squamous-cell carcinoma that I think was incidental. I cannot rule out a metastasis to the scrotum because skin metastases are not uncommon with bronchogenic carcinoma and a metastasis may be more differentiated than its primary tumor.

DR. KRANES: Probably the extreme leukocytosis was due to the necrosis?

DR. CASTLEMAN: Yes; that is quite common with tumors of the lung. There was a great deal of necrosis.

CASE 36522

PRESENTATION OF CASE

A thirteen-year-old boy entered the hospital because of a tumor of the jaw.

Eight weeks prior to admission the patient suddenly complained of a tender mass in the left side of the face that was painful when he opened his mouth. He was seen by his physician, received a dose of penicillin and was then referred to a dentist, who found impacted teeth that he believed were unrelated to the mass. A second dose of penicillin was given a week later, and the pain and the swelling of the cheek subsided. However, he was sent to the hospital for biopsy and further evaluation.

In the past he had had measles, mumps and chicken pox; otherwise he had been in excellent health. He had always drunk pasteurized milk.

The family history was noncontributory.

Physical examination revealed a well developed and well nourished boy. A bony-hard mass was attached to the angle of the left jaw that was prominent externally but did not extend into the mouth and was not palpable as a mass on the medial aspect of the bone at all. There was no difficulty in opening the jaw or protruding the tongue. There were a few freely movable discrete cervical lymph nodes on both sides.

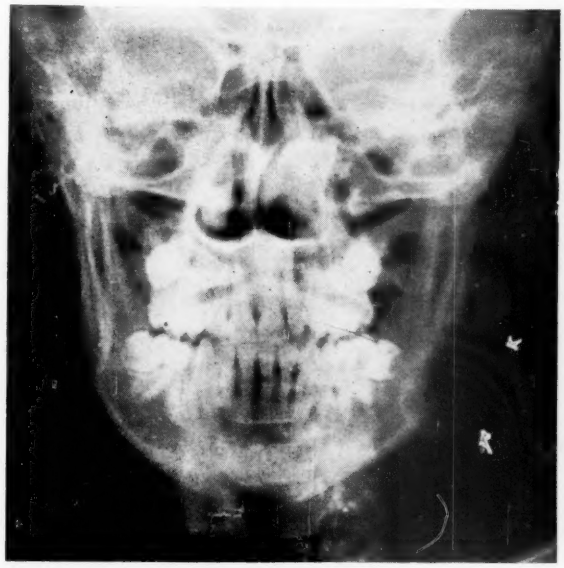

FIGURE 1. *X-Ray Film of the Jaw (Anteroposterior View). Arrows point to the outline of the lesion.*

The temperature was 97°F., the pulse 82, and the respirations 20. The blood pressure was 110 systolic, 80 diastolic.

Examination of the blood revealed a hemoglobin of 15.3 gm. and a white-cell count of 17,600, with 89 per cent neutrophils, 5 per cent lymphocytes, 5 per cent monocytes and 1 per cent eosinophils. The urine was normal. The serum phosphorus was 4.8 mg., and the alkaline phosphatase 10.6 units per 100 cc. There was insufficient serum for a calcium determination.

X-ray films of the mandible showed a 3-cm. expansile lesion situated at the angle of the left mandible (Fig. 1 and 2). The cortex was displaced laterally, and broken through in one large area. There appeared to be some small strands of bone remaining in the expanded portion, and there was also soft-tissue swelling adjacent to the lesion. The third mandibular molars bilaterally were unerupted and horizontally impacted. Examination of the long bones and pelvis failed to demonstrate any other bony abnormality. A chest film was normal.

On the second hospital day an operation was performed.

Differential Diagnosis

Dr. Kurt H. Thoma*: May I see the x-ray films?

Dr. James J. McCort: The expansile lesion described in the protocol is seen in the angle of the mandible. The cortical bone surrounding the lesion is thinned and bulges outward with a break in the cortex at one point. A few spicules of bone lie within the soft-tissue tumor causing the expansion. The lesion itself appears to be separated from the root of the third molar. Soft-tissue extension is noted (Fig. 1 and 2). The long bones and pelvis and the chest are normal.

Figure 2. *X-Ray Film of the Jaw (Lateral View). Arrows point to the outline of the lesion.*

Dr. Thoma: In view of the history, one would perhaps first think of osteomyelitis. The white-cell count was increased, particularly the polymorphonuclear leukocytes, which were 80 per cent. The fact that the patient had pain and that on penicillin administration the swelling improved might also point to infection. However, it is questionable whether two injections of penicillin one week apart would do much good in such a case. Against chronic or acute osteomyelitis is the fact that no cause either local or general could be found. The patient had no injury so that no hematogenous spread could have taken place. There was no trismus, which is generally present in infection, and there was no fever. The lymph nodes that were enlarged and might indicate infection were in the cervical region rather than in the submaxillary region, and furthermore they were on both sides, which probably means that they had been caused by some other condition, such as a cold or tonsillitis.

The next conditions that I might consider are various types of tumors. The first is the giant-cell tumor. A central giant-cell tumor occurs in the mandible of a young person. However, the angle of the jaw is not a common place; they occur most frequently in the anterior part of the mandible. There was no trabeculation, which is frequently present in giant-cell tumors, and the mass was not of the lobulated type; this was probably not a giant-cell tumor.

Ewing's tumor occurs in young persons and also is often seen in single form, becoming multiple later. The angle of the jaw is the site where Ewing's tumor has been found in other cases. Pain is often an early symptom and is generally followed by localized swelling. With Ewing's tumor there is often a leukocytosis although the ratio is not changed as it was in this case. The x-ray picture looks very much like an osteomyelitis; the cortex of the bone may be destroyed as it was in this case, and the tumor frequently develops both inside and outside the bone. There is often an onionskin appearance of the periphery of the bone, which was not present in this case. The new bone is generally parallel to the surface.

The third tumor that should be considered is a fibrosarcoma or perhaps an osteogenic sarcoma. The fibrosarcoma occurs frequently in young people. The 4 cases that I have heard about or have seen were in patients seven, seven, nineteen and twenty-one years of age. Fibrosarcoma frequently produces a very painful lesion. I have a patient who had a fibrosarcoma in the neck of the condyle that was as painful and as sensitive as this lesion was. Fibrosarcoma produces an osteolytic lesion with indefinite margins; it is expansive, and it occurs very frequently in the angle of the jaw. Fibrosarcoma may arise from one of three sources. It may be neurogenic, osteogenic or odontogenic. The neurogenic tumors develop from the tissue around the mandibular nerve, which in this case was in the region of the tumor. The odontogenic tumors form from the tooth germ. Some of them are purely epithelial — adamantinomas; others are purely mesenchymal

*Member, Board of Consultation, Massachusetts General Hospital; formerly, chief, Dental Service.

— fibromas, myxomas and fibrosarcomas; and some are mixed odontogenic tumors that contain structures of both types. Some of these tumors produce only soft-tissue lesions, whereas others produce calcified portions that simulate other tissue. I am fascinated by the fact that this tumor arose in the region of the apex of an unerupted third molar that had an open pulp canal. One could theorize that the tumor arose from the mesenchymal tissue at the apex. If this was the case, the tumor could have been either a fibroma or a fibrosarcoma, particularly the latter. I would favor as the diagnosis either Ewing's tumor or fibrosarcoma.

DR. MCCORT: The Radiology Department members had considerable difficulty in deciding whether the tumor was benign or malignant. We decided it was benign. Dr. Hanelin, who read the films, raised the question of eosinophilic granuloma or fibrous dysplasia. I believe you reported a case of eosinophilic granuloma in 1944,[1] Dr. Thoma.

DR. THOMA: Yes; I did. That patient, however, had the usual signs of Schüller–Christian disease. He suffered particularly from diabetes insipidus, with polyuria, nocturia and a tremendous thirst. He also had multiple bone lesions. I believe that most of the cases of eosinophilic granuloma or Schüller–Christian disease in the jaw generally have multiple lesions, and the granulomas frequently occur beneath developing teeth.

CLINICAL DIAGNOSIS

Giant-cell tumor.

DR. THOMA'S DIAGNOSIS

Ewing's tumor or fibrosarcoma.

ANATOMICAL DIAGNOSIS

Eosinophilic granuloma of mandible.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: Dr. Ernest M. Daland, who operated upon this patient, unroofed the site of the lesion and was able to remove a fair amount of granular, somewhat gelatinous material that on microscopical examination was packed full of eosinophils. It probably was the most beautiful eosinophilic granuloma that we have ever seen in an early stage. There were no old, fat-filled cells, which are usually seen in the later stage of the disease. We have seen eosinophilic granuloma any number of times as a single lesion, especially in the ribs or other parts of the body, but I do not recall that we have ever seen it in the mandible before as a single lesion.

DR. THOMA: I have not.

DR. CASTLEMAN: The case you reported had several lesions, I believe.

DR. THOMA: Yes. That patient was given x-ray treatment by Dr. Sosman both to the jaw and to the pituitary gland. I heard later from his physician that he had made a complete recovery. He had also had a lesion about the size of a fifty-cent piece in the parietal bone of the skull that cleared up too.

A PHYSICIAN: Has any case been treated with ACTH alone?

DR. CASTLEMAN: I do not know. A case[2] was recently reported in which a lesion in the rib was observed by x-ray over a period of eight years and then was excised. In that case the individual lesion remained stationary for eight years, and no lesion appeared in any other part of the body.

REFERENCES

1. Thoma, K. H. Eosinophilic granuloma with report of one case involving first the mandible, later other bones, and being accompanied by diabetes insipidus. *Am. J. Orthodontics* (Oral Surg. Sect.) **29**:641-651, 1943.
2. Grant, A. R., House, R. K., and Crandell, W. B. Eosinophilic granuloma of rib: report of case observed for eight years. *New Eng. J Med.* **240**:541-543, 1949.

NEW HAMPSHIRE MEDICAL SOCIETY

PROCEEDINGS OF THE ONE HUNDRED AND FIFTY-NINTH ANNIVERSARY

House of Delegates, September 10, 1950 (Continued)

The report of the State Blue Shield Committee was then presented as follows:

> The desirability of improving relations between the Blue Shield organization and the medical profession has been quite apparent for some time. In that connection the Society's increased activity in the fields of education and public relations provided the natural step for inclusion in an over-all plan that of development of these relations.
>
> On April 23 the president, Dr. John P. Bowler, addressed a letter to each county-society president in which he pointed out:
>
> > There is a feeling among the membership that it would be advisable to have more active participation by our membership in the policy-making determinations of Blue Shield. The officers and directorate of Blue Shield share in this feeling; and after discussing the matter with them, it seems desirable to set up what we will name for the present as the Blue Shield Committee.
> >
> > As an interim matter, to be confirmed, modified or eliminated at the next annual meeting of the Society, we are proceeding on the basis of such a committee to consist of ten members, one representative from each county society. At this time I am asking the president of each county society to appoint his representative in order that the committee may get under way. At the next meeting of each county society, it would be practical for each society at that time to decide by what method a representative is to be named.
> >
> > It is hoped that a closer liaison will be established between the Blue Shield and the county society membership by this method.
>
> The first meeting was held May 14 as a combined meeting with the Directors of Blue Shield. Subsequent meetings were held May 18 and June 22.
>
> County representatives, each appointed by his respective county president, include: Belknap, Douglas Walker, M.D., of Laconia; Carroll, Francis J. C. Dube, M.D., of Center Ossipee; Cheshire, John N. Meany, M.D., of Keene; Coos, Edward M. Danais, M.D., of Berlin; Grafton, Everett C. Campbell, M.D., of Woodsville; Hillsborough, Richard T. Mulvanity, M.D., of Nashua; Merrimack, Thomas A. Ritzman, M.D., of Concord; Strafford, Jesse M. Galt, M.D., of Dover; Sullivan, Bernard P. Haubrich, M.D., of Claremont; Rockingham, Frederick S. Gray, M.D., of Portsmouth.
>
> The committee serves four basic functions: it gives physicians greater opportunity to participate in Blue Shield policy making; provides a clearing house where physicians can bring mutual Blue Shield and medical profession problems; provides for closer co-operation between Blue Shield and physicians; and, by utilizing county representation, serves as a professional consulting board for each county medical society and in turn, indirectly, for each hospital staff and physician interested in coordination and understanding of physician-patient needs so far as they may be developed through Blue Shield.
>
> This is to be regarded only as an interim report. Your committee is already in the process of conducting a survey of medical population in an effort to ascertain appropriate levels of surgical fees with a view toward ultimate revisions — if they appear necessary.
>
> EVERETT C. CAMPBELL

Dr. Everett Campbell, for the Blue Shield Committee, then stated that the motion had been made that the members of the Blue Shield Committee be taken in as directors of Blue Shield, and that that recommendation be passed on to the Blue Shield. If that were done, it would mean a revision of the by-laws of the Blue Shield, because the present constitution and by-laws did not permit that. He believed that the matter was being taken up at the Blue Shield meeting, or would be taken up at the next Blue Shield directors' meeting.

Many physicians believed that they were inadequately represented at Blue Shield headquarters. Dr. Campbell said that the Vermont committee, which corresponded to this, was planning to make the same recommendations for their group. Before any other action was taken definitely, there would be a joint meeting with the Vermont committee, at which there would be an effort to thrash out some of the common problems.

Dr. Campbell urged that everyone who had not sent in the answers to the questionnaires sent out send them in, in order that the Committee might get on to the work of the revision of the schedules.

Dr. Brown stated that the Committee on Officers' Reports had not heard about this additional matter and had not met since hearing it. He moved that the report of the State Blue Shield Committee be recorded in the minutes of the meeting.

This motion was duly seconded and was carried.

Dr. Brown then moved that the supplementary recommendations or actions of the State Blue Shield Committee be approved.

This motion was duly seconded and was carried.

The report of the Special Committee on the Formation of a Grievance Committee was then presented, as follows:

> Pursuant to a vote of the House of Delegates on January 22, 1950, the speaker of the House appointed a committee of three to look into the matter of a grievance or complaint committee with instructions to report its findings and recommendations at the annual meeting. As a result this committee was appointed, and its recommendations are as follows:
>
> Having considered the many aspects of medical-lay public relations and the obvious need for some organized committee within the framework of the Society to correlate, study, segregate and act upon written complaints, it is the consensus of this committee that a newly created board of supervisors of the New Hampshire Medical Society will serve a useful and valued purpose in strengthening the public relations of the Society since duties and obligations involved clearly vary from those functions assigned Councilors under the Constitution and By-laws.
>
> It is our suggestion that a board of supervisors be created by the House of Delegates of the Society as expeditiously as possible and not later than December 31, 1950; that the board, when formed, elect its own chairman; that meetings be called at the discretion of the chairman; and that

in order to put the plan in operation for the first year and to provide for some system of membership rotation the first five counties in the State by alphabetical designation, namely Belknap, Carroll, Cheshire, Coos and Grafton, elect one representative each in 1950 to serve a one-year term, and in 1951 and thereafter elect a representative each to serve a two-year term; that the Counties of Hillsborough, Merrimack, Strafford, Sullivan and Rockingham elect one representative each for a two-year term.

It is recommended that the board of supervisors have jurisdiction to investigate complaints concerning professional conduct and ethical deportment but have no final jurisdiction in a judicial way. Just as a grand jury would, the board will receive and pass its own judgment upon evidence, but it will have no authority to discipline any physician. It may at any time express its advice to a member of the Society on any matter pertaining to professional conduct.

Your committee suggests the following procedure for receiving, studying and settling complaints.

The board will receive complaints in writing only from any person, lay or professional. These complaints will be addressed to the secretary of the New Hampshire Medical Society, who will acknowledge all such complaints in writing, and will forward each complaint to the chairman of the board of supervisors. It will be the responsibility of the chairman upon receipt of each new complaint to determine whether the first investigation or action on the complaint should be by the whole board at a meeting called for that purpose, or by one or more of the members of the board individually. It shall be left to the discretion of the chairman as to whether a matter submitted to the board will be referred directly to a County Medical Society for action or disposition.

Both the complainant and the physician against whom the complaint has been made will be furnished with a written statement and explanation of the final decision of the board as soon as possible after the board has completed its investigation of the case, whether the board considers the case closed, recommends definite action, decides to file charges with a judicial body or submits the matter to a county medical society.

Immediately after each meeting of the whole board, the officers of the board will prepare and deliver to the executive office of the Society a memorandum suitable for inclusion in the *Bulletin* of the Society and for release to the newspapers and radio news services of the State, concerning the status of ethical deportment within the Society. If desired, such material may be made the subject of a special bulletin to the entire membership of the New Hampshire Medical Society. The board will also prepare quarterly reports of progress to the Board of Trustees and an annual report and recommendations to the House of Delegates. These, of course, will be general reports containing no specific confidential information.

Your committee recommends that the organization, development, functions and progress of the board of supervisors be publicized through usual news mediums and that the purpose of the board, to provide better public-relations, be maintained. It is further recommended that an announcement of the Committee's organization, its purposes and manner of operation be released to all newspapers, radio news services and other news mediums and that periodic repeat stories be encouraged.

If the board receives a complaint that its officers believe can be settled amicably and without any question of local bias, by the board of censors or the local grievance committee of a county medical society, it may refer the complaint directly to the local society with the consent of both complainant and the physician complained against.

Members of the board of supervisors will serve without remuneration except as provided for by the House of Delegates but may utilize the services of the Society's executive office whenever needed.

These suggestions by your committee are merely basic and are offered as recommendations to be considered by the board of supervisors when created by the House of Delegates. Nothing contained herein shall be construed as outlining definite procedures, rules or regulations, which in our opinion will best be formulated as a direct responsibility of the board.

ALBERT BARCOMB
WILLIAM PENHALE
CLARENCE DUNBAR

Dr. Brown for the Committee on Officers' Reports moved that the report of the Special Committee on the Formation of a Grievance Committee be recorded in the minutes of the meeting.

This motion was duly seconded and was carried.

The following report of the Committee on Mental Hygiene was then presented:

It must be stated that owing to unforeseen financial curtailment the New Hampshire Mental Hygiene and Child Guidance Clinic has not been able to fulfill all its obligations. The Winant Home has not been renovated to care for juvenile patients suffering from severe neuroses or severe emotional maladjustments who need to remain under supervision to obtain more thorough psychotherapy than can be obtained at infrequent visits to clinics.

It is this type of intensive, supervised therapy that is almost imperative with these patients in order to prevent a more serious type of mental illness, and often the prevention of criminalistic tendencies from becoming actualities.

It is becoming increasingly evident that juvenile delinquents must have the benefit of psychiatric study and methods of rehabilitation. This can only be accomplished when adequate facilities and properly trained personnel are provided by the State of New Hampshire.

A plan is now being devised in which the states of Vermont, Maine and New Hampshire are participating through committees appointed by the governors of these states, the building and maintenance to be proportionately shared by each state. It is obvious that this requires legislation by each state and such should be supported by the legislative body of the New Hampshire Medical Society.

If this plan actually becomes a fact and the facilities are to be built within New Hampshire boundaries, Dr. John L. Smalldon, superintendent of the New Hampshire State Hospital, should have a large supervisory capacity of such facilities and personnel.

Another problem in which this society should interest itself is that of appropriate facilities for the care of sexual psychopaths. At present when a person has been examined, has had a hearing and has been adjudged by the courts to be of this type, the only available recourse for the courts is to commit him to the State Hospital for treatment.

It did appear, when this act was voted upon at the last legislature, that the intent was to provide a separate institution with its own personnel. However, funds were not appropriated. The law is obviously a step in the right direction to treat these persons from a psychiatric viewpoint. However, it is equally obvious that the State Hospital is not at present equipped to receive these cases, who are coming in increasing numbers, and to segregate them from those with other types of mental illness. At present there are fourteen in a ward that accommodates only sixteen and in which cases sent by the courts for observation of sanity have to be detained, as well as persons at the State Prison who have developed psychoses that require special psychotherapy. Accordingly about 50 per cent of these patients termed sexual psychopaths must be cared for in other wards.

As regards mentally deficient persons provision should be made for admission of children under five years of age, but in order to accomplish this it is a *must* that suitable quarters be provided and adequate increase of personnel be given the superintendent, Dr. Connelly.

Another survey, which seems necessary, is that of all epileptics in the State, and those found unable financially to obtain treatment, should be able to seek this at clinics provided for that purpose. An electroencephalograph is available at the State Hospital to any physician who wishes to obtain such an aid in the diagnosis of a suspected

epileptic or in determining the value of treatment that has been prescribed by the physician.

It is with gratification that we have learned that a special committee has been appointed by this society for the study of alcoholic patients, and that the State has also the service of a trained psychiatrist who will be able to conduct clinics for these unfortunates, because many can be successfully treated without admission to any hospital. If facilities are provided in general hospitals and Antabuse given, with continued follow-up treatment at clinics by a psychiatrist, many of these alcoholics may be greatly helped in their effort to cure themselves.

It is also gratifying to note an increase in indigent persons attending mental clinics, which have been provided through the efforts of Dr. John L. Smalldon, superintendent of the New Hampshire State Hospital. These clinics are held once each month at Nashua, Manchester, Portsmouth, Rochester and Keene. If any physician wishes to refer any mentally ill who are indigent, the hospital will be only too glad to furnish them the data available for such. The State Hospital offers all advanced types of therapy for the mentally ill who come for treatment, including group therapy — one of the more modern types of therapy.

It is proper here to inform this society that the State has been most fortunate in obtaining the services of such a highly trained psychiatrist and administrator as Dr. John L. Smalldon for the superintendency of the New Hampshire State Hospital.

Another step in mental hygiene has been taken by the warden at the State Prison in that each person sent there by the courts is interviewed by a psychiatrist and proper evaluation of his personality obtained, together with tests by a psychologist to assist the psychiatrist in his evaluation. This is a step in the right direction to assist in the rehabilitation of those members of society who have committed some crime.

As members of the New Hampshire Medical Society we can take just pride in this state's efforts and results for keeping in the van of any program that other states may have provided for the promotion of mental hygiene in its broad sense. Likewise it behooves us as a medical society to give full support to these programs that have been or will be initiated that have a practical value for mental hygiene.

ARTHUR B. HOWARD
SIMON STONE
EDWARD S. MORRIS

Dr. Brown then moved that the report of the Committee on Mental Hygiene for the year 1950 be recorded in the minutes of the meeting.

This motion was duly seconded and was carried.

The preliminary report of the Blood Bank Committee and the final report were then presented, as follows:

This report is submitted on the basis of incomplete returns but the number of complete questionnaires received is such that a general impression gained now should not be significantly altered by complete returns.

Two groups of questionnaires were circulated. The first was sent to all physicians in the State aimed at gaining the sense of the state organization on the desirability of having some sort of co-ordinated blood-bank program. The questionnaire also aimed at determining what sort of sponsorship would be most desirable for such a blood program. The second questionnaire went to hospitals and aimed at establishing the picture of blood utilization in the State.

Of 640 circulars sent to members of the Society, 157 were returned; 143 stated that they were in favor of a co-ordinated blood-bank program, and of these, all but 11 favored a Red Cross sponsorship; 14 were opposed to any sort of centralized program.

Of the circulars sent to the hospitals all but 5 were returned. Forty blanks were sent out. Of the 35 returned 8 institutions used no blood. The returns, then, represent those from 27 hospitals. A discussion of the questions will be taken roughly in the order in which they appeared on the questionnaire.

In all, 4627 transfusions were given in 1949 in the 27 hospitals reporting. Nine hospitals gave over 100 pints; 6 hospitals between 30 and 100 and 12 hospitals 30 or less. The 9 hospitals giving over 100 transfusions accounted for 4087 of the total. Six hospitals giving between 30 and 100 pints gave 373 transfusions. Considering the total population of the State our figures indicate that roughly 1 transfusion was given for each 105 persons in the State. This is considerably below the national figure of 1 transfusion for 40 persons. In terms of hospital admissions 1 transfusion per 14 admissions was given, as compared to 1 transfusion per 5 hospital admissions the country over; 467 units of plasma were given. The 9 hospitals using the greatest majority of the blood used only 159 units of plasma, indicating the decrease in the plasma use with increased use of blood.

Nearly all hospitals bleed donors and obtain the great majority of their blood used in this way. In 5 hospitals some blood is obtained from other hospitals or large blood-procuring agencies. One hospital obtains all its blood from a neighboring hospital. All but 1 hospital gave transfusions in which Rh-factor determinations were done on both donor and recipient. The total transfusions given under circumstances where no Rh factor was determined amounted to 10. In 2 hospitals no serologic tests for syphilis were carried out. One of these, however, utilizes the state laboratory. The total of transfusions in which no serologic tests were performed was 10. Two hospitals stated that they did not group blood, but still cross-matched blood.

Blood was stored in only 9 institutions. These institutions used 3819 of the 4637 transfusions given. In these hospitals there was 1 transfusion per 8 hospital admissions. The remaining hospitals used 808 pints of blood and averaged 1 transfusion per 42 admissions. This appears to indicate an increase in the use of blood where it is stored ready to use.

Only 6 institutions give out blood for use by individual physicians or other hospitals, and in all institutions the practice was an unusual one. This indicates a lack of any system of interchange of blood between hospitals or any setup to take care of transfer of blood from one institution to another in case of disaster. Twenty of 27 hospitals examine and take history on donors. The 7 hospitals that do not account for 391 transfusions or 8 per cent of the total — 8 per cent is a high figure for blood transfusions where no steps are taken to eliminate donors with history of jaundice, undulant fever or malaria. Ten more institutions keep no record of this examination. In institutions where examinations are made physicians carry these out in 15 of 20 instances. Technicians make the examination in the remaining 5.

In hospitals storing blood the average number of bottles stored at one time is 14. The range is 1 to 48 pints; 703 pints of blood were discarded for one reason or another. This represents 12 per cent of the total blood drawn and is quite comparable to the experience of other institutions the country over. Twenty-five institutions prepared plasma from outdated blood compared to 2 that did not.

Equipment came from 3 companies with 24 institutions using that of 2 leading companies. Twenty-four of 27 institutions used disposable sets for drawing blood, and 25 of 27 used disposable sets for giving blood to patients. Only 6 hospitals had refrigerators, the primary use of which was blood storage. Twelve shared a refrigerator used for other purposes. Fifteen hospitals stated that the temperature of the refrigerator was held between 2 and 10°C. Other hospitals did not answer this question.

All but 1 hospital believed that they had adequate personnel for cross-matching blood. Technicians registered with ASCP did this work for 11 institutions. In 11 others full-time, nonregistered technicians performed this function. In 4 institutions cross-matches were done by part-time technicians. The charge for blood varied from $25 to $30, 13 institutions charging the former price and 3 the latter. In 7 institutions no charge was made for blood. The price for plasma was extremely varied over the range of $15 to $25 per 250-cc. units. In 8 hospitals there are replacement schemes for paying for blood.

In 19 no such arrangement is made. In only 4 hospitals was a separate charge made for processing blood and for the blood itself. In 1 institution it was possible to cancel this separate charge by replacement of 1 extra pint of blood. Fourteen hospitals stated that their blood supply was adequate to meet the need. Thirteen hospitals did not answer this question. There were 15 answers concerning the question of supervision of the blood program. Thirteen stated that a physician was in charge. Two stated that some other person was in charge of the program, but did not specify what his capacity was. Of the physicians in charge of blood banks, 4 were anesthesiologists, 4 pathologists, 2 internists, 2 "physicians," and 1 did not answer the question.

Note: The northern counties of New Hampshire, Coos and Grafton, will soon be supplied with blood by the Vermont Regional Red Cross Blood Bank. Plans are laid to expand other Red Cross blood programs to service the remainder of New Hampshire. Some time will be required to activate this scheme should it be requested by the physicians of southern New Hampshire. A complete report will be returned to the secretary of the state organization upon complete returns from the hospital questionnaire.

JOHN B. HOLYOKE
HOWARD L. ELLIOT
CLINTON R. MULLINS

In May, 1949, the Blood Bank Committee was appointed to determine the status of blood-transfusion therapy in New Hampshire and to investigate the advisability and means of promoting a co-ordinated state-wide blood program.

To this end two groups of questionnaires were circulated. The first, sent to all physicians in the State, was aimed at gaining the sense of the state organization on the desirability of having some sort of co-ordinated blood-bank program. The questionnaire also aimed at determining what sort of sponsorship would be most desirable for such a blood program. The second questionnaire went to hospitals and aimed at establishing the picture of blood utilization in the State.

Of 550 circulars sent to members of the Society, 158 were returned. One hundred and forty-four stated that they were in favor of a co-ordinated blood bank program, and of these, all but 11 favored a Red Cross sponsorship. Fourteen were opposed to any sort of centralized program.

Of the 40 circulars sent to hospitals, all were returned. Of the 40 institutions, 8 used no blood. The returns, then, represent those from 32 hospitals where blood was used. A discussion of the questions will be taken roughly in the order in which they appeared on the questionnaire.

In all, 5742 transfusions were given in 1949 in the 32 hospitals using blood. Twelve hospitals gave over 100 pints; 7 hospitals between 30 and 100, and 13 hospitals 30 or less. The 12 hospitals giving over 100 transfusions accounted for 5233 of the total. Six hospitals giving between 30 and 100 pints gave 431 transfusions. Considering the total population of the State, our figures indicate that roughly 1 transfusion was given for each 93 persons. This is considerably below the national figure of 1 transfusion for 40 persons. In terms of hospital admissions, 1 transfusion per 11 admissions was given as compared to 1 transfusion per 5 hospital admissions the country over. Four hundred and ninety-four units of plasma were given in 31 hospitals. Of the hospitals responding to this question, the 11 using the greatest majority of the blood used only 186 units of plasma.

Nearly all hospitals bled donors and obtained the great majority of their blood used in this way. In 6 hospitals some blood was obtained from other hospitals or large blood-procuring agencies. One hospital obtained all its blood from a neighboring hospital. All but one hospital gave transfusions in which Rh-factor determinations were done on both donor and recipient. The total transfusions given under circumstances where no Rh factor was determined amounted to 10. In 2 hospitals no serologic tests for syphilis were carried out. One of these, however, utilized the state laboratory. The number of transfusions in which no serologic tests were performed was 10. Two hospitals stated that they did not group blood but did cross-match blood.

Blood was stored in only 12 institutions. These institutions used 4856 of the 5742 transfusions given. In these 12 hospitals there was 1 transfusion per 8 hospital admissions. The remaining hospitals used 884 pints of blood and averaged 1 transfusion per 30 admissions. This indicates an increase in the use of blood where it is stored ready to use.

Only 8 institutions gave out blood for use by individual physicians or other hospitals, and in all institutions the practice was an unusual one. This indicates lack of any system of interchange of blood between hospitals or any setup to take care of transfer of blood from one institution to another in case of disaster. Twenty-five of the 32 hospitals examined and took histories on donors. The 7 hospitals that did not accounted for 391 transfusions, or 7 per cent of the total. Seven per cent is a high figure for blood transfusions where no steps were taken to eliminate donors with a history of jaundice, undulant fever or malaria. Twelve more institutions kept no record of this examination. In institutions where examinations were made, physicians carried these out in 18 of 24 hospitals. Technicians made the examination in the remaining 7.

In hospitals storing blood, the average number of bottles stored at one time was 14. The range was 1 to 48 pints. Seven hundred and twenty-six pints of blood were discarded for one reason or another. This represents 12 per cent of the total blood drawn, and is comparable to the experience of institutions the country over. Twenty-seven institutions prepared plasma from outdated blood, compared to 2 that did not.

Equipment came from 3 companies with 27 institutions using that of 2 leading companies. Twenty-seven of 31 institutions used disposable sets for drawing blood, and 29 of 31 used disposable sets for giving blood to patients. Only 9 hospitals had refrigerators whose primary use was blood storage. Fifteen shared a refrigerator used for other purposes. Eighteen hospitals stated that the temperature of the refrigerator was held between 2 and 10°C. Other hospitals did not answer this question.

All but 1 hospital believed that they had adequate personnel for cross-matching blood. Technicians registered with ASCP did this work for 11 institutions. In 15 others, full-time, nonregistered technicians performed this function. In 4 hospitals cross-matches were done by part-time technicians. The charge for blood varied from $25 to $30, 15 institutions charging the former price and 3 the latter. In 8 hospitals no charge was made for blood. The price for plasma was extremely varied over the range of $6.45 to $36.00 per 250-cc. units. In 10 hospitals there were replacement schemes for paying for blood. In 22 institutions there was no such arrangement made. In only 7 hospitals was a separate charge made for processing blood and for the blood itself. In 1 institution it was possible to cancel this separate charge by replacement of 1 extra pint of blood. Seventeen hospitals stated that their blood supply was adequate to meet the need. Fifteen hospitals did not answer this question. There were 17 answers concerning the question of supervision of the blood program. Fifteen stated that a physician was in charge. Two stated that some other person was in charge of the program, but did not specify what his capacity was. Of the physicians in charge of blood banks, 6 were anesthesiologists, 4 pathologists, 2 internists, and 2 "physicians," and 1 did not answer the question.

From this report we can conclude that:

Many of the physicians in the State are not certain of the advisability of a co-ordinated program for New Hampshire. Of those reaching a conclusion, the great majority are in favor of such a co-ordinated operation and believe that the American Red Cross is a satisfactory agency to institute such an operation.

Blood utilization in New Hampshire is considerably below that the country over.

Institutions having a ready source of blood utilize more per admission than institutions where this agent is not so accessible.

Blood administration in most institutions is under adequate guidance and given with adequate care. There are some startling exceptions to this fact.

There is no standardization in the various hospitals of technic, equipment or type of personnel concerned in blood-transfusion therapy.

There is little interchange of blood from institution to institution.

There is no adequate setup for blood procurement in case of disaster.

It is likely that certain federal agencies will designate the American Red Cross as the agent to obtain necessary correlation and co-operation of all agencies interested in blood procurement in case of disaster. In addition to the information gained from these questionaires, the events of last year, other questionnaires and queries made from other sources have yielded information that the committee believes should be included in this report.

Coos and Grafton county medical societies have elected to join the Burlington Regional Blood Center under the auspices of the American Red Cross. It is planned that other Red Cross programs now in existence will be made available to the physicians of the remainder of the State within the next year should each county medical society choose to use this service. Before such a blood program can be instituted, each county medical society must give its approval. It has been the experience of other medical groups that, in the face of the institution of a Red Cross program, from the start the closest possible supervision by the medical profession is imperative if the program is to be satisfactory. All counsels indicate that, regardless of type of blood program developed, existing banking facilities should not be disrupted. Each institution that now draws blood must remain as a potential source of blood in case of disaster, with the resulting extreme call for this therapeutic agent.

At present several official agencies in the State are studying the problem of the defense and disaster planning. In none of these groups, except those sponsored by the Society, is there representation of persons closely associated with blood programs. In conclusion, the committee recommends that the House of Delegates accept this report and the following recommendations:

That the Society actively stimulate the various county societies to reach a decision on the advisability of choosing the American Red Cross to sponsor a coordinated blood program for the remaining counties of the State that are not already served by this agency.

That the Society act to aid in the formation of some other program should the decision of the county societies be to reject the Red Cross sponsorship.

That the Society accept the following contentions: that no blood bank at this time be inactivated as a result of the institution of any type of centralized program; that any such centralized program act to supplement the supplies of those banks already in operation; that a close liaison between this committee and the Committee on National Emergency Medical Service be established by having at least one person common to both groups; that the Civil Defense Advisory Council of the Governor include in its membership a member of the Society; and that the Blood Bank Committee continue its activities throughout the next year and be given the prerogative of acting as the agent of the Society in an advisory capacity to carry out the recommendations outlined in this report.

Dr. Brown moved that the preliminary and final reports of the Blood Bank Committee, as outlined, and of the recommendations of the Blood Bank Committee be adopted.

This motion was duly seconded and was carried.

Dr. Sven M. Gundersen then presented the interim report of the Committee on Arthritis and Rheumatism, as follows:

The Committee actually has done no work so far and has had no meetings. This is due to two things. First, the Scientific Committee of the New England Chapter of the Arthritis and Rheumatism Foundation has had only one meeting, earlier this year, and it did not seem appropriate to institute any work on the state level until the New England Regional Committee had formulated definite plans.

The second reason is that there is a peculiar situation in this state because of the prior existence of the New Hampshire Society for Crippled Children and Handicapped Persons. It is my intention to consult Dr. Ursula Sanders, of the Crippled Childrens' Division of the State Board of Health, and Mr. Orr and Mr. Gregg, of the Society for Crippled Children and Handicapped Persons, as soon as possible to explore the possibility of close cooperation between their organizations and our committee prior to launching any work on arthritis clinics in the State. I think it would be a pity if these various organizations were working at cross purposes when it seems obvious that many of our objectives are along the same lines.

Dr. Brown, for the Committee on Officers' Reports, moved that the interim report of the Committee on Arthritis and Rheumatism be included in the minutes of the meeting.

This motion was duly seconded and was carried.

Dr. Brown then moved a recess until after the Golf Dinner.

This motion was duly seconded and was carried.

Whereupon the meeting was recessed at 6 o'clock in the afternoon.

The meeting of the House of Delegates reconvened at 10 p.m. on September 10, 1950, with B. Read Lewin, speaker of the House, presiding.

The following delegates answered the roll call:

The President, *ex-officio*
The Vice-President, *ex-officio*
The Secretary-Treasurer, *ex-officio*
Roger P. Brassard, Laconia
W. J. Paul Dye, Wolfeboro
Ralph W. Tuttle, Wolfeboro (alternate for Francis J. C. Dube)
Albert C. Johnston, Keene
Louvane A. Fox, Keene
Julius Israel, Berlin
Marjorie Parsons, Colebrook
Everett C. Campbell, Woodsville
Reginald K. House, Hanover
Leslie K. Sycamore, Hanover
Leslie E. McKinlay, North Haverhill
Harris E. Powers, Manchester
Richard T. Mulvanity, Nashua
Raymond H. Marcotte, Nashua
Frank F. Flagg, Nashua
Edward D. Hagerty, Manchester
Lloyd L. Wells, Manchester (alternate for Oscar Burns, Milford)
Warren H. Butterfield, Concord
Edward V. Putnam, Warner
William D. Penhale, Concord
Francis Brown, Henniker
Frederick S. Gray, Portsmouth
Louis C. Theobald, Exeter
Henry Saltonstall, Exeter
Albert E. Barcomb, Rochester
Addison Roe, Newport
Pauline Spear, Claremont (alternate for B. Read Lewin, Claremont)

The speaker declared a quorum present, and the meeting proceeded.

The report of the Committee on Amendments to the Constitution and By-laws was then presented, as follows:

No new copies of *Charter and Amendments — Constitution and By-laws of the New Hampshire Medical Society* have been printed since 1935. The Committee is now in the process of having typewritten a copy of this bringing in all changes and amendments that have occurred within the past fifteen years. This required a considerable amount of time in research through previous state meetings and transactions by Dr. Deering G. Smith, secre-

tary, and, in turn, considerable work by this committee to transcribe a new copy up to date including all changes, striking out omissions and renumbering chapters and sections.

Inasmuch as these critical times have called for more changes to be considered this year, it seems inadvisable to have copies of the above printed until after the annual meeting in September, when probably more changes will be instituted than at any other one individual session of the House of Delegates.

It is obvious from the above that present considered changes cannot be referred to by chapter, article, section, line and word. For purposes of consideration of the members of the New Hampshire State Medical Society, the following have been suggested:

That there be a succession of officers to the presidency in order that the President shall be well indoctrinated in the responsibilities, problems, and procedure of the office. That the Vice-President shall be elected by written ballot at the annual meeting of the House of Delegates and shall succeed without further balloting the following year to President-Elect and the next year to President.

That there be established an executive committee consisting of the immediate Past-President, the President, the President-Elect, and the Vice-President, the Secretary-Treasurer, and the Speaker of the House of Delegates.

That the office of secretary-treasurer be divided between two men — one to be secretary and the other to be treasurer. Inasmuch as the Society voted to have an executive secretary, since the demands of this office are too time consuming and detailed for a physician in active practice in these times, that the work of the Secretary is largely in an advisory and corresponding capacity, and so with minimal duties, the salary of the latter be proportionally reduced considering the amount of work now required. That dividing the secretary-treasurer office between two medical men would make for further participation by members of the Society in its activities and further distribute the work of these two offices.

That any member of the New Hampshire Medical Society who has been a member for fifteen years and is sixty-five years old or over shall be elected to life membership, on request of his County Society, provided he is no longer in active practice or that he is ill or physically disabled or in financial difficulties.

An elected delegate shall have been a member of the Society for the preceding two years before serving in the House of Delegates.

That the Executive Committee shall have the power to appoint interim committees, and to call special meetings of the House of Delegates or the Society, or both, and also to set the time, date and place for such meetings.

All other proposed changes are largely of a technical nature concerning wording and will be considered later. If any member of the Society has any further proposals along these lines or comments on what has been already proposed as mentioned above, kindly communicate with this committee.

W. J. Paul Dye
Loren F. Richards
Joseph E. Larochelle

Dr. Dye for the Committee stated that there had been no published changes in the *Constitution and By-laws* of the New Hampshire Medical Society since 1935. With a great deal of research by the Secretary and the Committee, these had been brought up to date, including all the revisions, and the printed record contained the *Constitution and By-laws*, up to July 1, 1950, with all the incorporated changes since 1935.

The proposed changes of the Constitution had to be reported at this time and then laid on the table for one year.

The proposed changes were as follows:

Article V of the Constitution. Change to read: "and (2), ex-officiis, the immediate Past-President, the President, the President-Elect, the Vice-President, and the Secretary-Treasurer."

Dr. Brown stated that the sense of this amendment was the addition of the President-Elect and the immediate Past-President. But the main thing was that subsequently in the Constitution a new officer was added to the Society's list of officers: the President-Elect.

The Committee on Officers' Reports recommended that the wording be changed throughout the amendment where the Committee on Constitution and By-laws had recommended it to read "and the Secretary-Treasurer" that it read "and the Secretary and Treasurer"; in that way, it was not specified that the Secretary and Treasurer must be different people. Furthermore, the President, in his report, and the Committee, after careful consideration, approved and believed it should read "Secretary and Treasurer."

Dr. Dye in the absence of the other members of the Committee accepted the suggestion.

In reply to a question regarding immediate disapproval of the amendments, Dr. Dye read Article 12, as follows:

The House of Delegates may amend any article of this Constitution by a two-thirds vote of the delegates registered at that annual session, provided that such amendment shall have been presented in open meeting at the previous annual session, and that it shall have been sent officially to each component county society at least two months before the session at which final action is to be taken.

He then stated that a great many members of the Society believed that there should be a succession of officers, in order to indoctrinate the President before he took office, and this succession of officers would constitute the Executive Committee, so that by the time a man became president, he would have been in executive session as a member of the Executive Committee and would have served as an officer for seven or eight years. Eventually, the Executive Committee would consist of the immediate Past-President, the President, the President-Elect, the Vice-President, the Secretary-Treasurer and the Speaker of the House. The only elected officer in the upper bracket would be the Vice-President, who succeeds the President-Elect after a year, the President-Elect succeeding the President. Actually, it would be only three years, but the other men would have had experience, and it is very possible that a vice-president who has been a speaker or a vice-speaker of the House would be selected.

If the amendments were disapproved, the action would be final, and if action were wanted some other time, it would have to be started all over again.

Dr. Dye moved the acceptance of the first change, in principle.

After considerable discussion President Bowler spoke as follows:

The office of Secretary-Treasurer has been discussed here. I make no apologies for discussing it, except there may be the point that an outgoing officer should perhaps be put to bed. On the other hand, I am going to be quite frank and I am going to say that I think that perhaps an outgoing officer has a right to his opinions about an experience such as we had this year. I am not asking for sympathy. But, I am going to say that I think it is only reasonable retribution that after the beating we have taken this year, and the situation with which we began as an officer, it was just about the weakest setup that I have ever seen.

I believe very strongly that what the Society needs is more individuals in the participation and the process of the indoctrination and a distribution among counties in a much better way. Let me put it this way: that it lessens the load on individuals. The important fact that a man is on the Executive Committee is not for the amount of work that his primary position may entail, but it is the distribution of responsibility.

I have no apologies whatever to make about the Executive Secretary situation. I think they have done a superlative piece of work. I am not worrying, and I did not worry and the Committee did not worry at the time when we had to get into something and move and not argue about it, but just do something, and we did not worry too much about the connection of the Woodbury situation. It was the best and the most economical situation that we could work out at that time, being committed as we were by the previous House of Delegates on a program of public-relations that we had to carry out and were carrying out but had not paid for. We walked in without any money to pay for it, and we walked into five thousand payables.

We did not do much worrying or wondering about whether or not that was a reasonable thing from the standpoint of relations. I think that it has worked out excellently. I think that this meeting is one evidence of it; this meeting has been prepared 99 per cent by two executive secretaries. There is no practicing physician who can do it.

If we are going to try to promote a public-relations program and all these things, there is going to be little choice in the matter. The world is not working our way.

There are things in the relations of the details that are not desirable; I believe that is a problem that can be worked out, also. It just does not mean that the thing is wrong. I am not concerned much about those details. I think there is something to be considered about the separation of the Secretary and the Treasurer, purely on the basis of an executive-committee setup, and for the participation and the representation on any executive committee I think it is important that the more people on the Committee, the better it is.

I had heard for a good many years, when I had no contact with the Society to any extent at all and I was never in the House, that this society had been run over the years as a one-man show. You have all heard it. Why don't you talk about it? Why was it so? It was not the individual; it was the system. But the individual is the fellow who took the rap. It was all because it sloughed along and nobody did a job except one man; there was no succession, no executive committee and no indocrination, and any man who went in as I did who knew nothing about it had no background whatever.

Then there is the question: Why should there be an executive secretary? Because the job will never be done otherwise.

So that what we are voting on, actually, is not whether we want an executive secretary or not, but what the program is going to be and the purpose of the Society. Because if it is to continue, there is only one way that it can continue, and that is with the people I have mentioned.

Another matter is the separation of the offices of Secretary and Treasurer. There is no sense in pussy-footing around it and putting this and that in, so that some day you may want to shift it. Let's meet it right on the nose. We vote now that we present or that we do not present at this meeting an amendment that will be acted upon next year.

I am not going to make any apologies for what I have said; it is without any reflections, and without personalities, because I wrote this in the report three months ago, and it is printed. All I am asking is that one who has been through this year in the Society, without anybody to pass the buck to may have just a little to say in the discussion here, so that we may decide it one way or the other. There are not going to be any "ahd's" for me on the basis that maybe some day it may or may not be; this is *it*, right now. We vote whether this is presented or not. If the vote is against it, that is the end of it for now.

But, from my experience, I say that this thing is important. I am quite sure that you cannot expect men to go into these jobs without this participation, and you are not going to have an executive committee that can carry the weight that it must carry without representation, and the more men you have in these offices, the better.

Dr. Marcotte stated that the work that Dr. Bowler had done during the past year was beyond reproach or criticism. He had had a very difficult year, owing principally to the illness of the former secretary and, secondly, the unhappy situation that had occurred at Manchester during the year.

Dr. Marcotte considered the necessity of dividing the offices of Secretary and Treasurer to be open to debate. Whether it was necessary or not and whether a much larger executive committee that might possibly become unwieldly was needed he did not know; there were quite a few members on the Committee at present, and there would be more, with the President-Elect, and with the Past-President. The necessity of an executive vice-president was also open to debate in his opinion. He regarded it as also debatable whether a man who devoted part of his time to a limited practice and part of his time to secretarial work, a man who knew the problems and could sympathize with the difficulties and help the Society through them should be chosen, or whether a layman who was totally alien to all the problems, should be chosen. He pointed out that the dues had been increased to a point where many men were grumbling. The bugbear of socialized medicine, in Dr. Marcotte's opinion, was certainly not so serious today as it had been two years ago, or formerly. If the problem became more imminent, outside help in the form of public-relations and an executive secretaryship might be needed. Other societies had engaged public-relations men, executive secretaries and so forth, but New Hampshire was a small state, with a limited membership.

Dr. Marcotte realized that Dr. Bowler had had no indoctrination, and that subsequent officers two years hence would begin to be indoctrinated and know what it was all about. If there was to be a secretary who sat on the Executive Committee with a former president, a president-elect and so forth, the size of the Committee would be formidable.

Speaker Lewin restated the motion before the House, that the change in Article V, as read, be presented to the General Session.

Dr. Hagerty moved that the amendment read "Secretary-Treasurer."

This motion was duly seconded and was lost, 9 voting for and 10 against the motion.

Speaker Lewin then called for a voice vote on the motion to be presented to the General Session.

There was a chorus of "ayes," and the motion was carried, with 3 dissenting votes.

Dr. Dye presented the next amendment to the Constitution, Article VIII, Section 1, to be changed to read as follows:

> "Section 1. The officers of this Society shall be a President, a President-Elect, a Vice-President, a Speaker and a Vice-Speaker of the House of Delegates, a Secretary and Treasurer, ten Councilors (one from each County), and a Board of three Trustees."

Dr. Brown, for the Committee on Officers' Reports, suggested another change: in conformity with the President's suggestion that the Councilors be elected by the counties, it was recommended that the parenthetical (one from each County) be changed to read "(one elected by each County)."

Dr. Sycamore asked how this change would affect the status of these men as officers of the Society.

Dr. Brown replied that they could still be defined in connection with Article VIII, Section 1, as officers of the Society, and could be elected in any way the House desired or could be appointed. This was the definition of officers of the Society. The Councilors were among the officers of the Society.

Dr. Johnston stated that if the Councilors were going to be officers of the New Hampshire Medical Society, he did not see how they could be elected by a county society. It might mean one other officer elected by the county societies who was an officer of the New Hampshire Medical Society.

Dr. Brown replied that there were none but that the Constitution could be amended.

Dr. Sycamore agreed in principle with the idea of having the Councilors elected by the county societies, but he thought that it was illegal for the New Hampshire Medical Society to have officers that were not elected by the New Hampshire Medical Society. He therefore moved that the motion be tabled until a clarification by legal counsel could be obtained.

This motion was duly seconded and, on a rising vote, was carried.

Dr. Brown, for the Committee on Officers' Reports, then moved that the recommendations of the Committee on Amendments regarding Article VIII, Section 1, as originally read by Dr. Dye, be presented to the General Session.

Dr. Marcotte asked if it would be possible to approve this, with the approval of legal counsel.

Dr. Dye replied that, apparently, the crux of the situation was whether the Councilors should be elected by the county societies or by the House of Delegates. He asked the speaker to get the opinion of the House by asking for a vote on how many favored election of Councilors by the county societies.

The speaker announced that the number for and against was about evenly balanced.

Dr. Johnston then spoke as follows:

> I never knew exactly what the purpose of the Councilors was until we called a special meeting at Concord, and I think I am correct in reporting or saying that Dr. Bowler himself was not exactly correct about what the Councilors were for. Our forefathers, our ancestors, who made that decision, made a very wise decision, in my opinion. They wanted to make sure that they had a body of men old enough and experienced enough in the medical society to decide issues that the younger men and the more hotheaded members might not be able to contend with, and this is the same sort of a setup that our government has in the Senate's being over the Congress. And, as you have probably noticed, the Councilors in the New Hampshire Medical Society have always been what we call the elderly men of the Society. They were picked because they had been through the crucible of experience.
>
> Now, if we are going to send this thing back to the county societies, I think that we shall defeat the purpose for which the Councilors were elected; if that is so, we do not need any Councilors, and we can take care of everything among the House of Delegates.

Dr. Dye agreed with Dr. Johnston's point. The Nominating Committee, of course, selected a man from each county to succeed the Councilor who was retiring. By and large, the Nominating Committee was composed at the moment of five members from different parts of the State. They were not intended to be stampeded by local feelings about Councilors, and there was a tendency to choose, as Dr. Johnston had said, the older men in various counties who had proved reputations and, from an ethical standpoint, sound judgment. Dr. Dye believed that there was a question about the advisability of electing Councilors from each county, particularly if the Council got to the point where it was exercising more functions than it had in the past, and personal elements might enter into the election by county societies, thereby defeating the purpose of older and wiser leaders on this particular body.

Speaker Lewin then asked that the motion be read before the vote.

The previous motion was then read.

The motion was carried, unanimously.

Dr. Dye then read the following amendment to Article VIII, Section 2, the first line being changed to read:

> The Vice-President shall be elected for a term of one year automatically succeeding thereafter to the offices of President-Elect and President for a term of one year. Succession shall also take place automatically upon the removal, resignation, retirement, or death of any officer.

After considerable discussion concerning succession to the office of president, Dr. Dye withdrew his motion.

Dr. Saltonstall then moved that the President-Elect succeed to the office of President.

This motion was duly seconded and was carried.

Dr. Dye pointed out that all the motions on the amendments to the Constitution were that the amendments be presented in open meeting, at a

general session of the Society. No final action was being taken by the House.

Dr. Saltonstall moved that the second sentence in Section 2 of Article VIII be changed to read as follows: "The Secretary and Treasurer and Councilors shall be elected."

This motion was duly seconded and was carried.

Dr. Brown then moved that Section 2 of Article VII be stricken out, because it was inconsistent with a proposal subsequently made by the Committee regarding the *By-laws*.

This motion was duly seconded and was carried.

Dr. Dye then recommended that Chapter I, Section 6, of the *By-laws* be changed to read as follows:

> Section 6. Any physician who has been a member of this Society for a term of fifteen years, and is either not less than sixty-five years of age, or partially or totally disabled, and to whom the payment of dues would be a financial hardship, on the request of his County Society, may be made a life member by a majority vote of the House of Delegates. Life Members shall have the same rights and privileges as other members, but shall not be required to pay dues.

Dr. Brown, for the Committee on Officers' Reports, recommended that the age of sixty-five years not be mentioned and that the reference to "disability or hardship" be replaced by the statement: "Any physician who has been a member of the Society, and is permanently retired from fully active practice, on the request of his county society and so forth."

After a lengthy discussion the question was called for.

Dr. Dye then moved the adoption of Chapter I, Section 6, as follows:

> Section 6. Any physician who has been a member of this Society for a term of fifteen years, and is either not less than sixty-five years of age, or partially or totally disabled, and to whom the payment of dues would be a financial hardship, on the request of his County Society, may be made a life member by a majority vote of the House of Delegates. Life Members shall have the same rights and privileges as other members, but shall not be required to pay dues.

This motion was duly seconded and was carried.

Dr. Dye then moved that in Chapter II, Section 1, of the *By-laws*, the following be added: "or as determined by the Executive Committee."

This motion was duly seconded and was carried.

Dr. Dye then moved that in Chapter III the corresponding sentence be changed to read as follows: "Each General Meeting shall be presided over by the President, or in his absence or disability, or by his request, by the President-Elect or by the Vice-President, in that order.

This motion was duly seconded and was carried.

Dr. Brown moved to strike out in Chapter III, Section 5, the word "Treasurer."

This motion was duly seconded and was carried.

Dr. Dye moved that the following change be made in Section 1, Chapter IV: "The first meeting of the House of Delegates shall be held whenever designated by the President and/or the Executive Committee . . ."

Secretary Smith suggested taking out the "and" so that the sentence would read "whenever designated by the President or the Executive Committee" and leaving out the 7:30 time.

Dr. Dye accepted the change.

Dr. Brown for the Committee on Officers' Reports, moved that, with that change, the change in Section 1, Chapter IV, be adopted.

This motion was duly seconded and was carried.

Dr. Dye then moved that in Chapter IV, Section 2, the word "Treasurer" be stricken out.

This motion was duly seconded and was carried.

Dr. Brown moved that as much of Section 2, of Chapter V, reading "at the first meeting of its annual session" be stricken out.

This motion was duly seconded and was carried.

Dr. Dye then moved to strike out "President and" and "President or" in the same Section 2 of Chapter V.

Dr. Brown moved the insertion, each time, the words "President-Elect and Vice-President" and "President-Elect or Vice-President" in the sixth and eighth lines on page 63 of the printed record.

This motion was duly seconded and was carried.

Dr. Saltonstall moved that, because the changes in Section 2, Chapter V, could not be settled legally, the matter be dropped, and the discussion of the next chapter proceeded with.

This motion was duly seconded and was carried.

Dr. Saltonstall then moved that any mention of the word "President-Elect" in the *By-laws* to date be deleted from the record.

This motion was duly seconded and was carried.

Dr. Dye moved that all mention of all changes relative to "Secretary and Treasurer" mentioned up to the present time in the *By-laws* be omitted.

This motion was duly seconded and was carried.

Dr. Dye then mentioned a proposed change in "Chapter VII, Section 5 — a new section" concerning a grievance committee.

After considerable discussion Dr. Wells moved that the matter of the grievance committee be referred back to the Committee on Amendments to the Constitution and By-laws. The motion was duly seconded and was carried.

Dr. Dye voted that, inasmuch as the Executive Committee did the work of the Committee on Public Relations, Section 1, Chapter VIII, be changed by the deletion of "Committee on Public Relations" and the substitution therefor of "an Executive Committee."

Dr. Brown suggested that the Committee on Publications also be deleted.

Dr. Dye accepted the suggestion about the Committee on Publications.

Dr. Brown then moved that both committees be deleted in Chapter VIII, Section 1.

This motion was duly seconded and was carried.

Dr. Dye then recommended that Section 6 of Chapter VIII be changed to read as follows:

> The Executive Committee shall consist of the immediate Past-President, President, Vice-President, Secretary-Treasurer, Speaker of the House of Delegates, and Vice-Speaker. . . [down through "Annual session" after which add," or at other designated times]."

Dr. Brown moved the adoption of the change.

This motion was duly seconded and was carried.

Dr. Dye then moved to add:

> The President shall be Chairman of this Committee. The Committee shall administer and/or advise concerning the affairs and policies of the Society and may designate the time and place for special and regular meetings of the House of Delegates and of the Society as a whole.

This motion was duly seconded and was carried.

Dr. Dye recommended further in the same Section the following addition: "It shall prepare the annual budget for submission to the House of Delegates."

Dr. Brown, for the Committee on Officers' Reports, moved that this change be adopted.

This motion was duly seconded and was carried.

Dr. Brown, for the Committee on Officers' Reports, then moved that the following be added:

> It may employ such secretarial staff as is necessary for the proper conduct of the Society's affairs. It shall keep records of its transactions, to be reported to the House of Delegates. It shall prepare the Budget for the ensuing calendar year, for submission to the House of Delegates at its annual meeting.

This motion was duly seconded.

Dr. Sycamore moved an amendment to the motion, to strike out the word "annual meeting" and have it read "to report the budget to the House of Delegates."

This amendment to the motion was duly seconded and was carried.

The original motion, as amended, was then carried.

Dr. Dye then recommended the following change in Chapter IX, Section 4, of the *By-laws*: deletion of the statement "all of which shall be at all times accessible to every member of the New Hampshire Medical Society."

Dr. Smith moved that Section 4, Chapter IX, second line, be changed to read: "He shall be required to keep a record of the proceedings of the Committee," all the second sentence of Section 4 being deleted.

This motion was duly seconded and was carried.

Dr. Dye moved that the following change, in Chapter X, Section 2, be approved: deletion of the clause "approved by the House of Delegates on a call of the ayes and noes," and substitution therefor of "by a majority vote of the House of Delegates."

This motion was duly seconded and was carried.

Dr. Dye then moved that the meeting be adjourned until Tuesday morning at 8:30 o'clock.

This motion was duly seconded and was carried.

Whereupon the meeting of the House of Delegates was adjourned at 1:10 a.m. on September 11, 1950.

(To be concluded)

The New England Journal of Medicine

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REPORT ON THE BRITISH NATIONAL HEALTH SERVICE

After six weeks of on-the-scene study and observation, a group of five distinguished physicians reported to the American Medical Association on medical care in Great Britain under the National Health Service.[1] This comprehensive appraisal provides a history of the evolution of governmentally controlled health services, summarizes the major provisions of the current legislation and passes judgment on the operation of the Act to date. A few errors in the presentation of certain facts should, however, be noted.

Complete medical care has not, as stated in the report, been provided by the school health system for all school children, thus unjustifiably excluding the general practitioner from this part of his contact with the families under his care. The school medical authorities merely carry out periodic examinations and immunizations and make recommendations to the family doctor, who after discussion with the parents handles them as he sees fit. The further statement that the number of doctors in training as specialists greatly exceeds the number needed is true, but no evidence is submitted to support the contention that "this means insecurity for those that now hold hospital appointments." In fact, one might perhaps more justifiably say that the past and present systems in Great Britain have given the consultant too much permanence of tenure, as contrasted with the more flexible method in this country. Nor does there appear to be a well founded basis for the generalization that consultants, with patients still waiting to be seen, "now stop when they have completed their three and one-half hour session" — the period for which they are paid. Highly debatable, also, is the statement that "the seriously ill and problem cases are crowded out of the large general hospitals by minor cases that should be filtered out in a general practitioner's office or in an outpatient department." It is the experience of many specialists that patients who enter such hospitals do require consultant care but that the facilities for hospitalization are inadequate to meet the need. The further allegation that the Act "has to a large extent destroyed private practice" is true only so far as general practice is concerned. The overwhelming majority of specialists are working for the Ministry of Health on a part-time basis and receiving payment now for the care of patients, most of whom, in the days before the Act, they treated free of charge. In addition, they carry on private practice much as before, although presumably with a smaller total number of cases, owing to the reduced levels in the higher income brackets.

One other improvement, not mentioned in the report, may have followed as a consequence of the Act. By virtue of a more tightly knit organization of the country into *regions* of several million people each, a better caliber of care by specialists in communities under 100,000 in population may be evolving. No critical evidence on this point in Great Britain has been adduced, however. Indeed, the tactic in some places there of placing more weight

on satisfying the capricious requirements of the examiners for the advanced degrees at the Royal Colleges than on years of studied experience may vitiate some of the possible advantages of integration, as happens when green young men who hold the degrees are appointed to replace capable older practitioners who do not. Moreover, in this country, without benefit of Government intervention, plans with similar advantages have been put on trial. In New York, the Commonwealth Fund has sponsored a scheme for organizing a sizable part of that state into the orbit of the University of Rochester. The Bingham Associates have accomplished the same end by putting the facilities of Tufts College Medical School at the disposal of the State of Maine.

Although these minor disagreements with the report seem justified, a host of incisive criticisms in that account appear to have a frightening validity. The provision of all aspects of medical care free of charge has led to ludicrous abuses. As an example of the outrageous demands made with exasperating frequency, a British consultant on a recent visit in Boston cited the instance of a man seen on a home visit. The consultant recommended prompt hospitalization and offered to take the patient there in his own car. The man, although fully ambulatory and in no pain, insisted on an alleged statutory right to an ambulance and got it. Indeed, the Ministry has rejected the concept of part or token payment for *any* of the essential services, a concept that would protect against some fraction of such unreasonableness. The Ministry is unwilling to charge even as little as a shilling (14 cents) for each prescription, a situation that has resulted in the writing of 211,000,000 prescriptions — about 5 per person — during the twelve-month period ending June, 1950. Even so, the patient is not guaranteed the medication he needs. For three months a physician in Boston has been supplying propylthiouracil to an English friend in a London suburb who finally had to give up trying to get it by regular Health Service channels.

The hope has been expressed that once the novelty of free medical care has worn off, the needless visits to general practitioner and outpatient department will decline. After two years, however, the trend appears to be in the other direction. The parade of people — one can scarcely call many of them patients — through the doctor's office continues in alarming volume. The greater the rate at which they come, the more superficial the work he can do tends to become. Much of the time of this critically essential physician is given over to the signing of numerous certificates and the filling-in of reports related in some direct or highly indirect way to health. A host of other personnel in the special services have appropriated to themselves parts of his former contribution to diagnosis, therapy and preventive medicine, to the extent that many British no longer refer to the family physician as Doctor, but use only his surname. Furthermore, the general practitioners have been to an increasing degree cut off from the stimulus of association with a hospital, even to the point of being unable to follow the course of their own patients. It is amazing that under such stifling influences they can maintain any interest at all in clinical medicine, and it is a tribute to their moral stamina that they have not given up completely. The British Medical Association, moreover, surveying a group of 5251 doctors, found that 30 per cent had net incomes of less than 1000 pounds, the average being 500 pounds, and that 39 per cent had net incomes between 1000 and 2000 pounds, with an average of 1500 pounds. In a series of conversations with a dozen different visiting British physicians, not one has been encountered who defends the dispositions in their country with respect to the general practitioner.

The attitude of the Minister of Health toward the medical profession has been a source of continual irritation, so much so that, according to the *Lancet* there was, at a recent meeting of the British Medical Association, "warm response to each charge of bad faith against the Minister of Health or his Ministry." Indeed the pages of the *Lancet* as well as of the *British Medical Journal* have, for the last two years, bristled with vitriolic comments attesting to the validity of such charges as that the Minister has broken his promises, has introduced lay control into many phases of medical activity and has centralized the control of virtually all aspects of the Service, including the individual hospital-management committees.

In its attempt to provide something for everyone, the Ministry has spent on dental and ophthalmic services a sum equal to that of the whole general-practice service, a vast expenditure supplying countless people with free glasses, appliances and dentures while patients with serious illnesses that could possibly be ameliorated or cured lie at home in their beds and die. The provision of care for major illness would seem a top priority in this country but not, unfortunately, under Mr. Bevan, who himself had to report that 4000 sorely needed beds in tuberculosis hospitals alone stood idle for lack of nurses.[2]

Many observers of the British scene have been amazed at the acquiescence of the medical profession in a scheme that the overwhelming majority had rejected in a formal poll before it went into operation. Direct questioning of many British doctors reveals that, when none of the three major political parties would espouse their cause, they considered their position hopeless. This appraisal seems a sound one and points a lesson to the profession in this country that bears re-emphasis. No matter how right its position is considered to be, it has little chance of prevailing in a democracy unless it can persuade the majority of the people to its way of thinking and keep them so persuaded. Its present trial by fire should help it burn out any of its own outmoded or erroneous patterns of thought or conduct.

Those who favor Government provision of medical care for the whole citizenry with no direct charge liken it to governmental provision of education for all children.[3] There are at least these pertinent major differences between the two tasks. In the first place, the child must have his education paid for by someone else, whereas most adults ought by their own productive efforts to be able to pay for their own medical care, especially if they utilize the insurance principle. The question can be fairly put: If, even in socialist Great Britain, the individual is expected to budget for his own breakfast, why should he not have a similar financial responsibility for his own health?

It is, moreover, reasonably easy to determine how advanced any child's education should be, but it may be exceedingly difficult to determine how much diagnostic and therapeutic effort a patient merits. One has the impression, in the first place, that it is basically unsound to shift the responsibility for recovery from illness to a state of full working capacity away from the sick person toward the Government. The medical profession, in its present state of ignorance, is unable to handle effectively such a responsibility on behalf of the Government, since it is unable in many cases to distinguish between those who do require medical services and those who do not, or who, after a bona fide illness, unduly protract their convalescence.

Nevertheless, the British Minister of Health, faced with the steady rise in costs of the National Health Service with each six-month period it has been in operation, is now calling upon the doctors themselves to protect his dwindling funds from the rapacity or casual importunity of numberless undeserving applicants. This dual role of intimate confidant of the patient and guardian of the public purse cannot logically be handled by the same agency. No Anglo-Saxon system of justice would permit the same person to act both as counsel for the plaintiff and as judge of the merits of the suit, and yet something analogous seems to be contemplated for the doctor in Great Britain.

It begins to look more and more as though the first person who must evaluate the significance of his symptoms is the one who has them. Instead of citizens of this country being urged to consult their physician at slight or no provocation, would it not be better to teach them which symptoms or signs command immediate professional attention, as stressed in such educational campaigns as those of the American Cancer Society? Conversely, when a new symptom appears to be identical with one that was present in the past and shortly vanished, should it not be pointed out that consultation with a physician is likely to result only in his temporizing to see if the same thing will happen again? One of the basic premises of Government and culture in this country appears to involve education of the individual to the use of a maximum degree of personal freedom and responsibility. One sees no need to depart from this premise, as the British

appear to be doing, when the problem of health is being considered.

References

1. Martin, W. B., Penberthy, G. C., Sanford, H. N., Bryner, U. R., and Peterson, C. M. Medical care in England under National Health Service: report to Board of Trustees of American Medical Association. *J. A. M. A.* **143**:1420-1434, 1950.
2. Parliament. Last stages of medical bill. *Lancet* **2**:231, 1950.
3. Davis, B. M. British National Health Service. *Pub. Health Rep.* **64**:161-191, 1949.

AMA TO THE RESCUE

THE most important problem that faces the medical schools of the country today is one that has justly given rise to grave concern. The increasing complexity of laboratory and clinical instruction, added to the economic distress of inflation, has made it impossible for many schools to see a rosy future under the system of deficit financing that circumstances have imposed on them. With the once green pastures of voluntary philanthropy become arid, federal aid has seemed to be the only recourse left available.

The risks of federal aid, however, with its inevitable effect on the tax burden and its ultimate threat to academic freedom are becoming more apparent than ever before in this country, and a strong reaction has set in against such a method of meeting current expenses.

At this point the timely action of the trustees of the American Medical Association in appropriating from the fund for education a half million dollars for the use of the medical schools comes like the arrival of reinforcements in a hard-pressed battle. This allocation of such a considerable sum of money in addition to the annual expenditures of the Council on Medical Education and Hospitals is no mere gesture in the interests of publicity; it is the very core of a new movement to preserve the independent teaching of medicine, the animadversions of the Committee for the Nation's Health to the contrary notwithstanding.

The action of the trustees will be particularly pleasing to the membership of the Massachusetts Medical Society — even to those fellows who have not yet paid their national dues — when they learn that it came as the result of a resolution presented to the Council in October, and adopted by the Committee on Medical Education of the Society in the following month.

This resolution, in brief, was as follows:

> That the Massachusetts Medical Society suggest to the Board of Trustees of the American Medical Association that a liberal amount of money (circa $500,000) be allocated from the National Educational Fund in 1951 for the medical schools of the United States . . . .

The announcement of this appropriation — representing chill penury to the Committee for the Nation's Health, accustomed to thinking in terms of federal largess — was greeted with the enthusiasm that might be expected, and was followed by a burst of voluntary contributions to augment it.

The appropriation, having its origin in the rank and file of the profession, sparked by the resolution prepared by a committee of the Massachusetts Medical Society, represents something more than another effort to block the advance of socialism. It represents a timely seizing of the initiative in the battle for independent thought and action, and a constructive step of the first magnitude on the part of the American Medical Association.

In view of this measure, the communication from DR. CURRENS printed elsewhere in this issue of the *Journal*, suggesting that the American Medical Association raise a medical education fund from the practicing physicians, takes on special significance.

PERIPATESIA

THE *Lancet*, having apparently settled its recent unpleasantness with the printing profession, during which it was down to a four-page issue, is back under a full head of steam, and is to be congratulated.

It is pleasant to welcome back also the *Lancet's* peripatetic correspondents, one of whom,* perhaps having rested from his peripatesia, perhaps having never been a complete victim of it, has indulged in some statistics relative to another mode of travel. His new car having a lock on the near-side door, he is compelled to slide a yard across the seat on entering or leaving it. With an average of 15 visits a day, Sundays and holidays included, and an initial entering and leaving the car at the beginning and end of the morning and afternoon rounds he finds that a simple equation ($17 \times 2 \times 365 \div 1760 = 7$)

*In England now. Running commentary by peripatetic correspondents. *Lancet* **2**:593, 1950.

shows that he now is doomed to slide 7 miles a year on the seat of his trousers, or resume a peripatetic type of practice.

Further statistical observations, this time of the dew-point on the drip-ends of clarinets, have revealed that, when these instruments are played in more than 5° of frost, icicles form that may stick into the necks of the cello players in front.

It is heartening to realize, occasionally, that pure research needs no ulterior motive.

Our moustached friends will be glad to learn that the London National and Military Gazette has made the discovery that the wearing of moustaches is conducive to health. It affirms that the moustaches, acting as a part of the breathing apparatus, absorb the cold of the air before it enters the nostrils, and are, consequently, a preservation against consumption.

Boston M. & S. J., *December 25, 1850*

Fourth-year students in approved medical schools are reminded of the *Journal's* prize essay competition for 1951.

For further information see *The New England Journal of Medicine*, September 28, 1950, p. 508.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR NOVEMBER, 1950

RÉSUMÉ

Disease	November 1950	November 1949	Seven-Year Median
Chancroid	2	4	3*
Chicken pox	862	927	927
Diphtheria	9	20	28
Dog bite	850	734	631
Dysentery, bacillary	5	8	9
German measles	83	33	66
Gonorrhea	189	206	378
Granuloma inguinale	0	0	0*
Lymphogranuloma venereum	1	0	0*
Malaria	0	1	15
Measles	156	141	657
Meningitis, meningococcal	3	3	6
Meningitis, Pfeiffer bacillus	4	5	5
Meningitis, pneumococcal	1	3	3
Meningitis, staphylococcal	0	0	0
Meningitis, streptococcal	0	1	0
Meningitis, undetermined	4	8	4
Mumps	588	385	461
Poliomyelitis	54	73	35
Salmonellosis	2	3	7
Scarlet fever	292	236	465
Syphilis	129	133	303
Tuberculosis, pulmonary	208	189	217
Tuberculosis, other forms	9	7	11
Typhoid fever	2	3	2
Undulant fever	2	1	4
Whooping cough	444	539	539

*Six-year median.

COMMENT

The only diseases notably above the seven-year median were German measles, mumps and poliomyelitis.

Below the seven-year median were chicken pox, diphtheria, bacillary dysentery, gonorrhea, measles, salmonellosis, scarlet fever, syphilis and whooping cough.

The 83 cases of German measles represented the highest incidence of this disease during the month of November in the past fifteen years.

Although the 54 cases of poliomyelitis were above the seven-year median, this number was distinctly below that reported in November, 1949.

The 9 cases of diphtheria represented the lowest November incidence in eight years, and the 2 cases of salmonellosis the least number reported in the past ten years.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Diphtheria was reported from: Arlington, 1; Cambridge, 1; Dedham, 2; Dunstable, 1; Greenfield, 1; Lowell, 2; Somerville, 1; total, 9.

Dysentery, amebic, was reported from: Newton, 3; total, 3.

Dysentery bacillary, was reported from: Boston, 2; Lowell, 1; Worcester, 2; total, 5.

Encephalitis, infectious, was reported from: Amherst, 1; Reading, 1; total, 2.

Hepatitis, infectious, was reported from: Canton, 1; Walpole, 1; Wrentham, 4; total, 6.

Meningitis, meningococcal, was reported from: Boston, 1; Weymouth, 1; Worcester, 1; total, 3.

Meningitis, Pfeiffer bacillus, was reported from: Boston, 1; Mansfield, 1; Newburyport, 1; Watertown, 1; total, 4.

Meningitis, pneumococcal, was reported from: Springfield, 1; total, 1.

Meningitis, mumps, was reported from: Framingham, 1; Watertown, 1; Weston, 1; total, 3.

Meningitis, undetermined, was reported from: Cambridge, 1; Plymouth, 1; Springfield, 1; Wellesley, 1; total, 4.

Poliomyelitis was reported from: Ayer, 1; Amherst, 1; Beverly, 1; Boston, 1; Brockton, 1; Chelsea, 1; Colrain, 1; Easton, 1; Fitchburg, 2; Framingham, 2; Greenfield, 1; Hanover, 1; Lawrence, 1; Lee, 1; Longmeadow, 1; Malden, 1; Medfield, 1; Medford, 2; Millis, 1; Natick, 1; New Bedford, 1; Newton, 1; North Brookfield, 1; Norwell, 1; Peabody, 2; Pittsfield, 7; Plympton, 1; Southbridge, 1; Springfield, 1; Swampscott, 2; Tewksbury, 1; Wayland, 2; Weymouth, 2; Ware, 1; Whitman, 1; Williamstown, 2; Worcester, 4; total, 54.

Psittacosis was reported from: Wellesley, 1; total, 1.

Salmonellosis was reported from: Boston, 1; Halifax, 1; total, 2.

Septic sore throat was reported from: Boston, 4; Pepperell, 4; Worcester, 1; total, 9.

Trichinosis was reported from: Brookline, 1; Worcester, 1; total, 2.

Typhoid fever was reported from: New Bedford, 1; West Bridgewater, 1; total, 2.

Undulant fever was reported from: Easthampton, 1; Templeton, 1; total, 2.

CORRESPONDENCE

A FUND FOR MEDICAL EDUCATION

To the Editor: Doctors are inclined to underestimate their responsibility to the community. We who are practicing medicine today are in a particularly fortunate position financially, and I only trust that the medical societies and particularly the American Medical Association realize this and take some concrete step to demonstrate their appreciation to the people.

I should like to suggest that the American Medical Association seriously consider raising a medical education fund from the practicing physicians to be used to help the medical schools in their present financial plight. If it were properly called to the attention of the doctors of the country that 75 per cent of the institutional cost of their medical education came from the public or philanthropy I believe each would be willing to make an annual payment for the support of such a fund. One hundred dollars from 100,000 practicing physicians would amount to $10,000,000, the approximate

amount of the annual deficit for medical education. I write to you concerning this since I was contemplating sending such a sum to my alma mater. It occurred to me, however, that there might be other schools much more in need of assistance than the one from which I graduated. The fair and just distribution of funds is always a problem but could be done quite equitably by a committee appointed by the American Medical Association or the Council on Education.

Such a fund would bolster the prestige of the American Medical Association tremendously in my opinion and it would help the medical schools to maintain their integrity.

JAMES H. CURRENS, M.D.

Boston

RESTORATION OF LICENSE

To the Editor: At the meeting of the Board of Registration in Medicine held on October 19, 1950, it was voted to restore to Dr. Louis L. Hoff of Holyoke his registration to practice medicine in the Commonwealth.

GEORGE L. SCHADT, M.D.
Secretary

State House
Boston

ADDITIONAL REFERENCE

To the Editor: Through an oversight, my paper entitled "Thromboangiitis Obliterans in Women," which appeared in the August 24 issue of the *Journal*, failed to include a reference to an excellent presentation of 25 cases by Dr. Samuel Silbert in an article entitled "Further Experience with Thromboangiitis Obliterans in Women" (*Am. Heart J.* **36**:757-771, 1948).

EDWARD A. EDWARDS, M.D.

Boston

BOOK REVIEW

Practical and Theoretical Aspects of Psychoanalysis. By Lawrence S. Kubie, M.D. 8°, cloth, 252 pp. New York: International Universities Press, Incorporated, 1949. $4.00.

The primary objects of this book, especially as they apply to the explanation of the practical aspects of psychoanalysis, have been admirably accomplished. It will certainly remove many of the uncertainties and misconceptions patients have before submitting to psychotherapy. The physician who has occasion to refer a prospective patient, and even the psychiatrist who must have satisfying answers for the inevitable questions of his patient, whether they are based on financial considerations, theoretical persuasions or basic resistances, will find his work made easier by referring to the explanations and examples propounded with such clarity.

Much emphasis has been placed on the impersonal role the psychoanalyst must play. His passive attitude in handling the positive and the negative transference situations might lead one to believe that the analyst is an unemotional, mechanical figure, noncensoring to be sure, but living in a paternalistic ivory tower. Dr. Kubie makes it very apparent that the therapist has himself been through the emotional stresses of life and has made his peace with his own doubts, problems and conflicts. He is therefore amply prepared to act as the resonance organ for the patient's own emotional conscious and unconscious forces.

The unending stream of popular psychologic "fiction" that is appearing can only serve to confuse even further the already perplexed minds of many people struggling for relief from emotional tension. This small book, however, deserves a widespread circulation. It would be entirely safe and fruitful in the hands of anyone receiving or requiring psychoanalytic therapy.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Public Health is People: An institute on mental health in public health, held at Berkeley, California, 1948. By Ethel L. Ginsburg. 8°, cloth, 241 pp. New York: Commonwealth Fund, 1950. $1.75.

This volume comprises a report of an institute on mental health in public health, held at Berkeley, California, in 1948, under the joint sponsorship of the California State Department of Health and the Commonwealth Fund. The faculty consisted of 8 psychiatrists, 3 pediatricians with psychiatric training and 5 public-health leaders. The "student body" was made up of 30 health officers drawn from city and county health departments throughout the state. The course consisted of lectures, meetings for discussion and clinics. The topics included the application of dynamic concepts of emotional growth and development, motivation of behavior, common human needs and the nature of interpersonal relations to the responsibilities and the everyday job of the health officer and his staff.

The report should be in all collections on mental and public health.

Handbook of Obstetrics and Diagnostic Gynecology. By Leo Doyle, M.S., M.D. 12°, cloth, 240 pp., with 45 illustrations by Ralph Sweet. Palo Alto, California: University Medical Publishers, 1950. $2.00.

The purpose of this small handbook is to present in a most concise form the essential features of obstetrics and gynecologic diagnosis. The material is well arranged, and there is a good index. The publishing is good, except that important tables are printed on the inside covers, where they are subject to wear and destruction.

Chemical Developments in Thyroidology. By William T. Salter, M.D., professor of pharmacology, Yale University School of Medicine. 8°, cloth, 87 pp., with 6 illustrations. Springfield, Illinois: Charles C Thomas, 1950. $2.00.

This small monograph discusses the thyroid hormone and the application of radioactive iodine. A long bibliography concludes the text and there is a good index.

The ABC of Acid-Base Chemistry: The elements of physiological blood-gas chemistry for medical students and physicians. By Horace W. Davenport. Third edition. 8°, paper, 86 pp., with 41 illustrations and 27 tables. Chicago: University of Chicago Press, 1950. $2.00.

This synopsis has been designed for medical students and physicians and has been in successful use for a number of years at Harvard, Utah and other medical schools, where it has been found that students could attain a working knowledge of the subject in about two weeks.

The Nose: An experimental study of reactions within the nose in human subjects during varying life experiences. By Thomas H. Holmes, M.D., Lester N. Hofheimer Research Fellow in Medicine; Helen Goodell, B. S., research fellow in medicine; Stewart Wolf, M.D.; associate professor of medicine; and Harold G. Wolfe, M.D., professor of medicine (neurology), Cornell University Medical College. With a foreword by Warfield T. Longcope, M.D. 12°, cloth, 154 pp., with 37 illustrations. Springfield, Illinois: Charles C Thomas, 1950. $4.50.

In this monograph the authors report the results of a study of disturbances in nasal and respiratory physiology occurring in response to a variety of stimuli. It was found that changes in the nose rarely occurred but that the deeper respiratory passages, other structures in the head and even other organs were involved. The various chapters discuss nasal physiology in general and the range of nasal functions in normal

subjects, and the alterations in nasal function following disturbances to other organs and functions, including the eyes and the deeper respiratory structures, the organism's pattern of adjustment to environment (fear, dejection, anger and anxiety) and the relation to gastric function and to sexual function. The last two chapters describe mechanisms involved in disorders of the nasal and paranasal spaces, and pain from the nasal and paranasal structures — the mechanism of "sinus headache." The observations were carried out on human patients. There is a good index, and the publishing is excellent. The monograph should be available to all persons interested in respiratory diseases and psychosomatic medicine.

NOTICES

ANNOUNCEMENTS

Dr. Lester M. Abelman announces the opening of an office for the practice of pediatrics at 201 Lexington Street, Belmont.

Dr. George D. Cutler announces the removal of his office to 92 Highland Street, Milton.

Dr. Edward M. Langer announces the removal of his office for the practice of internal medicine to the Van Skike Building, Sarasota, Florida.

Dr. George M. Pike announces the removal of his office from 474 Beacon Street to 137 Bay State Road, Boston.

HARVARD MEDICAL SOCIETY

A meeting of the Harvard Medical Society will be held in the Bigelow Amphitheater, Massachusetts General Hospital, on Tuesday, January 9, at 8 p.m.

The program, presented by the departments of Neurology, Neurosurgery and Psychiatry, Massachusetts General Hospital, (Dr. Stanley Cobb presiding), will be as follows:

Brain Abscess: Summary of Clinical and Pathological Findings. Dr. E. P. Richardson, Jr.

Radioactive Potassium: A New Isotope for Brain-Tumor Localization. Drs. Bertram Selverstone and William H. Sweet.

Preliminary Observations on Mental Abnormalities Occurring in the Course of Therapy with ACTH and Cortisone. Drs. Lincoln D. Clark and Stanley Cobb.

BOSTON CITY HOSPITAL HOUSE OFFICERS' ASSOCIATION

The Boston City Hospital House Officers' Association will present the following lecture as a part of its evening lecture series:

Tuesday, January 9. 7 p.m. Acute Renal Insufficiency. Dr. Homer Smith. Discussers: Dr. Maurice Strauss, chief, Medical Service, Cushing Veterans Administration Hospital; Dr. Robert Merrill, Peter Bent Brigham Hospital.

Wednesday, January 17. 4:30 p.m. Experimental Production of Microcytic Anemia. Dr. Maxwell Wintrobe, professor of medicine, University of Utah School of Medicine. Discussers: Dr. William Castle, director, Thorndike Memorial Laboratory, Boston City Hospital; Dr. Maurice Strauss, chief, Medical Service, Cushing Veterans Administration Hospital.

Attention is called to the time and date of Dr. Wintrobe's lecture.

NEW ENGLAND PEDIATRIC SOCIETY

A meeting of the New England Pediatric Society will be held on Wednesday, January 17, 1951. A scientific session will be conducted by Dr. Charles A. Janeway and members of his staff in the amphitheater of Building C, Harvard Medical School, from 2:30 to 5:00 p.m. At the evening meeting Dr. Laurence H. Snyder, dean of the Graduate College, University of Oklahoma, Norman, Oklahoma, will speak on the subject "Medical Genetics and the Pediatrician."

BAY STATE SOCIETY FOR THE CRIPPLED AND HANDICAPPED

On February 21, 1951, the Bay State Society for the Crippled and Handicapped, Inc., will hold a one-day rehabilitation conference at the Copley Plaza Hotel in Boston.

The morning meeting will include a discussion and demonstration of the Bay State Society Rehabilitation Projects in Springfield, Worcester and Boston. The luncheon speaker will be Mr. Eugene J. Taylor, New York City field representative of the National Society for Crippled Children and Adults, editorial-staff member of the *New York Times* and associate professor, Department of Physical Medicine and Rehabilitation, New York University College of Medicine. In the afternoon, there will be a demonstration clinic showing what is being done in rehabilitation, conducted by Dr. George G. Deaver, attending physician in physical medicine at the Lenox Hill Hospital, New York City.

NATIONAL RESEARCH COUNCIL, COMMITTEE ON HUMAN REPRODUCTION

The Committee on Human Reproduction of the National Research Council will hold its annual two-day conference on January 19 and 20, 1951, at the Hotel Commodore, New York City. The subject for this year will be pregnancy wastage. The list of speakers will include G. W. Anderson, of Johns Hopkins Hospital; L. Baumgartner, of Cornell University Medical College; L. E. Casida, of University of Wisconsin; G. W. Corner, of Carnegie Institution of Washington; S. H. Clifford, of Harvard Medical School; A. I. Csapo, of Carnegie Institution of Washington; M. E. Davis, of University of Chicago; A. T. Hertig, of Harvard Medical School; E. C. Hughes, of Syracuse University Medical Center; J. W. Jailer, of Columbia University College of Physicians and Surgeons; P. Levine, of Ortho Research Foundation; R. Nesbitt, of Johns Hopkins Hospital; E. Potter, of University of Chicago; E. Shorr, of Cornell University Medical College; H. C. Taylor, Jr., of Columbia University College of Physicians and Surgeons; C. Tietze, of National Committee on Maternal Health; C. A. Villee, of Harvard Medical School; and W. C. Young, of University of Kansas.

MISSISSIPPI VALLEY MEDICAL SOCIETY

The sixteenth annual meeting of the Mississippi Valley Medical Society will be held in Peoria, Illinois, on September 19, 20 and 21, 1951.

AMERICAN MEDICAL WRITERS' ASSOCIATION

The eighth annual meeting of the American Medical Writers' Association will be held at the Pere Marquette Hotel, Peoria, Illinois, on September 19, 1951, during the meeting of the Mississippi Valley Medical Society.

DAMON RUNYON SENIOR CLINICAL RESEARCH FELLOWSHIPS

The Committee on Growth of the National Research Council, acting for the American Cancer Society, is accepting applications for Damon Runyon Senior Clinical Research Fellowship. These fellowships in cancer research are financed by a grant of $110,000 from the Damon Runyon Memorial Fund to the American Cancer Society.

Applications should be filed before March 1, 1951, on behalf of the applicant by the institution where the fellow will be in residence. Applications will be considered in April, and fellowships ordinarily will begin on July 1, though this date may be varied at the request of the fellow. Awards are made directly to the institution on an annual basis, and renewal may be requested. Persons now holding these fellowships will be notified regarding applications for renewal.

Communications should be addressed to the Executive Secretary, Committee on Growth, National Research Council, 2101 Constitution Avenue, N. W., Washington 25, D. C.

(*Notices concluded on page xv*)

NOTICES (*Concluded from page 1066*)

SOCIETY MEETINGS AND CONFERENCES

JANUARY 3. Hampshire District Medical Society. Page 170, issue of July 27.
JANUARY 6. Massachusetts Society of Anesthesiologists. Page 1018, issue of December 21.
JANUARY 9. Springfield Academy of Medicine. Page 1018, issue of December 21.
JANUARY 9. Massachusetts Society of Anesthesiologists. Page 1018, issue of December 21.
JANUARY 9. Harvard Medical Society. Page 1066.
JANUARY 9. Boston City Hospital House Officers' Association. Page 1066.
JANUARY 11. The Diagnosis and Therapy of Lesions Producing Gastrointestinal Hemorrhage. Dr. Claude Welch. Pentucket Association of Physicians. 8:30 p.m. Haverhill.
JANUARY 17. Boston City Hospital House Officers' Association. Page 1066.
JANUARY 17. New England Pediatric Society. Page 1066.
JANUARY 19 AND 20. National Research Council, Committee on Human Reproduction. Page 1066.
JANUARY 22. Boston Lying-in Hospital Obstetric Round-Table Conference. Page 629, issue of October 19.
JANUARY 23. Norfolk District Medical Society. Page 629, issue of October 19.
JANUARY 31. American Academy of Orthopaedic Surgery (see Kappa Delta Award for Research in Orthopedic Surgery). Page 736, issue of May 4.
FEBRUARY 9. Beta Iota Chapter of Nu Sigma Nu. Page 1018, issue of December 21.
FEBRUARY 13. New England Society of Anesthesiologists. Page 512, issue of September 28.
FEBRUARY 21. Bay State Society for the Crippled and Handicapped. Page 1066.
FEBRUARY 27. Norfolk District Medical Society. Page 629, issue of October 19.
MARCH 5–8. New Orleans Graduate Medical Assembly. Page 1018, issue of December 21.
MARCH 26. Boston Lying-in Hospital Obstetric Round-Table Conference. Page 629, issue of October 19.
MARCH 27. Norfolk District Medical Society. Page 629, issue of October 19.
APRIL 9–13. American College of Physicians. Page 296, issue of June 15.
APRIL 10. New England Society of Anesthesiologists. Page 512, issue of September 28.
APRIL 24. Norfolk District Medical Society. Page 629, issue of October 19.
MAY 8. New England Society of Anesthesiologists. Page 512, issue of September 28.
MAY 9. Norfolk District Medical Society. Page 629, issue of October 19.
MAY 22–24. Massachusetts Medical Society. Annual Meeting. Hotel Statler, Boston.

DISTRICT MEDICAL SOCIETIES

HAMPSHIRE

JANUARY 3. 4:30 p.m. Veterans Administration Hospital, Northampton.
MARCH 7. 4:30 p.m. Cooley-Dickinson Hospital, Northampton.
MAY 2. 4:30 p.m. Annual Meeting. Jones Library, Amherst.

NORFOLK

JANUARY 23.
FEBRUARY 27.
MARCH 27.
APRIL 24.
MAY 9. Annual Dinner.

All meetings except the Annual Dinner will be held at the Boston Medical Library, 8 Fenway, at 8:00 p.m.

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, JANUARY 4

THURSDAY, JANUARY 4
*9:00–10:00 a.m. Cardiac Grand Rounds. Main Amphitheater, Children's Medical Center.
*9:00–10:00 a.m. Grand Rounds. Robert Breck Brigham Hospital.
*9:00–11:00 a.m. Medical Grand Rounds. Joseph H. Pratt Diagnostic Hospital.

FRIDAY, JANUARY 5
*9:00–10:00 a.m. Medical Conference. Joseph H. Pratt Diagnostic Hospital.
*9:00 a.m.–12:00 m. Combined Medical and Surgical Staff Rounds. Peter Bent Brigham Hospital.
*10:00 a.m. Surgical Clinic. South End Health Unit, 57 East Concord Street, Boston.
*1:30 p.m. Tumor Clinic. Out-Patient Department, Mount Auburn Hospital, Cambridge.

SATURDAY, JANUARY 6
*9:00–10:00 a.m. Surgical Grand Rounds. Joseph H. Pratt Diagnostic Hospital.

MONDAY, JANUARY 8
*11:30 a.m.–12:15 p.m. Clinical Conference. South End Health Unit, 57 East Concord Street, Boston. Dr. Cleaveland Floyd in charge.
*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.

TUESDAY, JANUARY 9
*12:15–1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.
*1:30–2:30 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children, Massachusetts General Hospital.
7:00 p.m. Boston City Hospital House Officers' Association.
8:00 p.m. Harvard Medical Society. Bigelow Amphitheater, Massachusetts General Hospital.

WEDNESDAY, JANUARY 10
*1:00 m. Clinicopathological Conference. Margaret Jewett Hall, Mount Auburn Hospital, Cambridge.
*1:00 m.–1:00 p.m. Clinicopathological Conference. (Children's Medical Center.) Amphitheater, Peter Bent Brigham Hospital.

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